Studies on Direct Functionalization of Aromatic Substrates

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CHAPTER 1

Introduction

Introduction

1.1. Direct formation of carbon-carbon bond

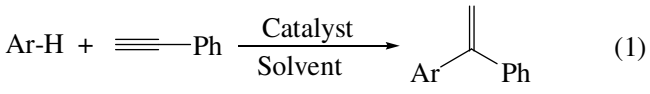
Direct formation of new **carbon-carbon** bond through the activation of aromatic **C-H** bond is an important method for the synthesis of various useful organic compounds[1]. The process gives a very simple, clean and economic method for the synthesis of various substituted aromatic compounds directly in one step from simple arenes, because in this process aromatic **C-H** bond directly acts as a functional group and it does not require the pre-functionalization like halogenation of aromatic **C-H** bond. This direct **carbon-carbon** bond formation method not only reduces the reaction steps but also avoids the use of **toxic** halogenated compounds. Historically, Friedel-Crafts reactions of aromatic compounds have been employed for the direct functionalization of aromatic compounds through the formation of new **carbon-carbon** bond, but these reactions require more than equimolar amount of a Lewis acid such as aluminium (**III**) chloride[2].

As a result, for over a century organic chemists have sought to develop new, clean and efficient, direct **carbon-carbon** bond forming methods[3]. To date, different methods have been developed for the direct formation of new **carbon-carbon** bond between arenes and olefins[4-8]. Of these differently developed methods **hydroarylation** and **iodoarylation** reactions are well known methods for the direct formation of new **carbon-carbon** bond between arenes and olefins.

1.2. Hydroarylation of alkynes

In the hydroarylation reaction, alkynes react with arenes and form arylalkenes in one step (**Scheme 1**).

Scheme 1



(1)

The resulting hydroarylation product is versatile intermediate in various organic syntheses. Recently, the hydroarylation reaction of olefins catalyzed by metals, acids and organometallic complexes has been reported as a popular method for the

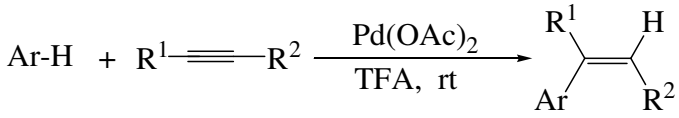
direct attachment of a carbon fragment to an aromatic ring[9]. Compared to the conventional synthetic methods, these newly developed methods have been improved with some fine properties such as a cheap catalyst, a small amount of catalyst and a short reaction time[10].

To date, many transition metal-catalyzed hydroarylation reactions of alkynes have been reported in the literature**.** A cursory glance at the results of the literature survey of the metal-catalyzed hydroarylation reaction of alkynes is given below.

1.2.1. Metal-catalyzed hydroarylation reaction of alkynes

Terminal and internal alkynes efficiently undergo hydroarylation reaction regio- and stereoselectively with different arenes in the presence of **Pd(II)** catalyst in trifluoroacetic acid (TFA) at room temperature and give thermodynamically less favorable *cis*-arylalkenes predominantly in most cases (**Scheme 2**)[10k,11]. The reaction represents a useful synthetic protocol to form *cis*-arylalkenes from electron rich arenes and alkynes in one step.

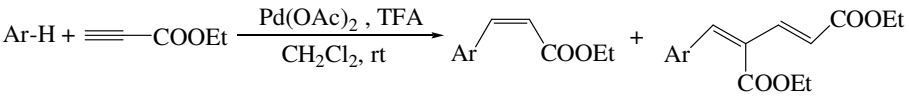
Scheme 2



(2)

On the other hand, the hydroarylation reaction of ethyl propiolates with arenes in the presence of **$Pd(OAc)_2$** in TFA and CH_2Cl_2 at room temperature gives diethyl (1*E,* 3*Z*)-4-arylbuta-1,3-diene-1,3-dicarboxylates along with the expected product ethyl(2*Z*)-cinnamates, although the yields of the buta-1,3-diene-1,3-dicarboxylates are low (**Scheme 3**)[10k].

Scheme 3

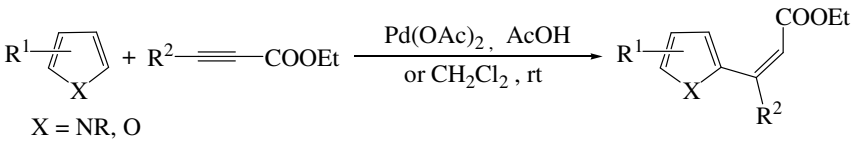


(3)

Alkynoates readily undergo hydroarylation reaction with heteroaromatic compounds such as pyrroles, furans and indoles at room temperature in the

presence of a catalytic amount of **Pd(OAc)$_2$** in acetic acid or dichloromethane and give *cis*-heteroarylalkenes in most cases (**Scheme 4**)[11a,c,d.6].

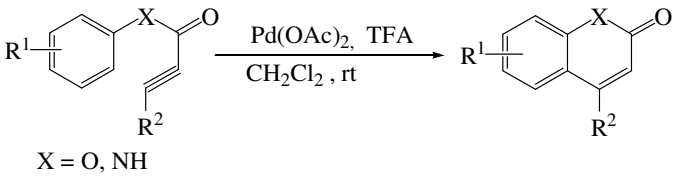
Scheme 4



(4)

On the other hand, arylalkynoates smoothly undergo intramolecular hydroarylation reaction in the presence of **Pd(OAc)$_2$** in TFA and CH_2Cl_2 at room temperature and afford coumarins and quinolinones (**Scheme 5**)[11a,d,e].

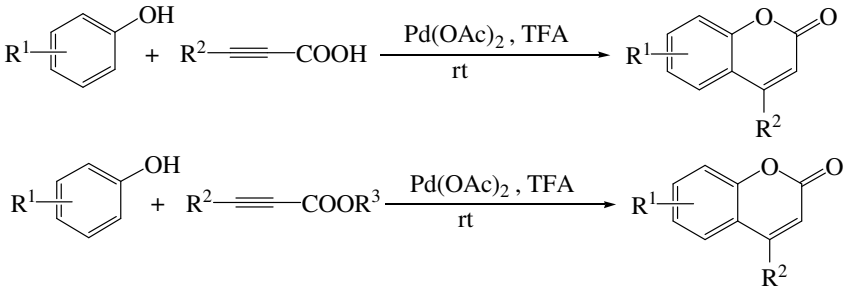
Scheme 5



(5)

Intermolecular hydroarylation reaction of propiolic acids and alkynoates with phenols in the presence of **Pd(OAc)$_2$** in TFA at room temperature gives coumarins (**Scheme 6**) [12].

Scheme 6



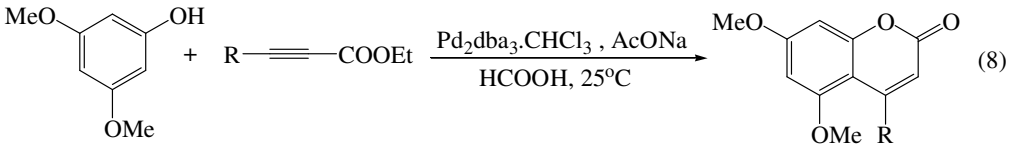
(6)

(7)

The **Pd**-catalyzed hydroarylation reaction is also applied to the synthesis of coumarins through the intermolecular hydroarylation of ethyl propiolates with electron rich phenols at 25^{o}C temperature[13]. In the presence of acetic acid solvent reaction does not proceed but in the presence of formic acid reaction proceeds

smoothly to afford the desire product. This may be due to the fact that formic acid converts **Pd(II)** to **Pd(0).** Actually, a **Pd(0)** species, **$Pd_2dba_3.CHCl_3$,** is an effective catalyst in both acetic acid and formic acid solvents although the latter solvent gives better results (**Scheme 7**).

Scheme 7

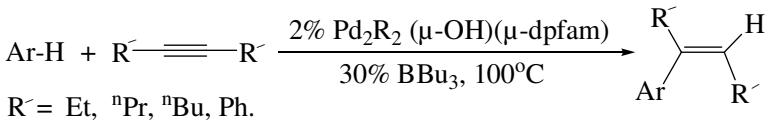


(8)

Recently, two palladium complexes such as **(IPr)$Pd(OAc)_2$** and **(IPr) $Pd(OCOCF_3)_2(H_2O)$,** (IPr=N,N'-bis(2,6-diisopropylphenyl)imidazol-2-ylidene) have been discovered that they catalyze the hydroarylation reaction under the same reaction conditions as **$Pd(OAc)_2$.** In the presence of these palladium complexes ethyl propiolates readily undergo hydroarylation reaction with arenes and selectively form cinnamates without the formation of the buta-1,3-diene-1,3-dicarboxylates (**Scheme 3**)[14].

Inoue *et al* reported that the dinuclear palladium complexes, **$Pd_2R_2(\mu\text{-}OH)(\mu\text{-}$ dpfam),** (**dpfam** = N, N' –bis[2-(diphenylphosphino)phenyl]formamidate, R= *p*-Tol or Me) in the presence of an additive trialkylborane catalyze the hydroarylation reaction of unactivated internal alkynes and selectively afford *cis*-products[15]. In the absence of the ligand **dpfam** the complex can not show the catalytic activity. Catalysts **$Pd(OAc)_2$** and **$Pd_2dba_3.CHCl_3$** are also inactive for the reaction (**Scheme 8**).

Scheme 8

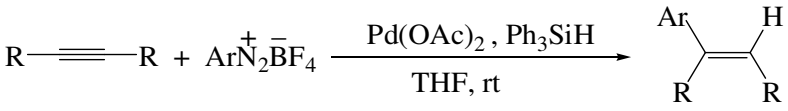


(9)

Cacchi *et al* reported that palladium catalyzed hydroarylation reaction of arenediazonium tetrafluoroborates with alkynes in the presence of triphenylsilane

affords stereoselectively hydroarylation products in moderate to high yields (**Scheme 9**)[16]. The reaction tolerates a variety of substituents including keto, ester, cyano, and nitro groups and can be performed as a one-pot procedure generating the arenediazonium salt in situ. With ethyl phenylpropynoate as the starting alkyne, the hydroarylation affords ethyl (*Z*)-2-arylcinnamates stereo- and regioselectively.

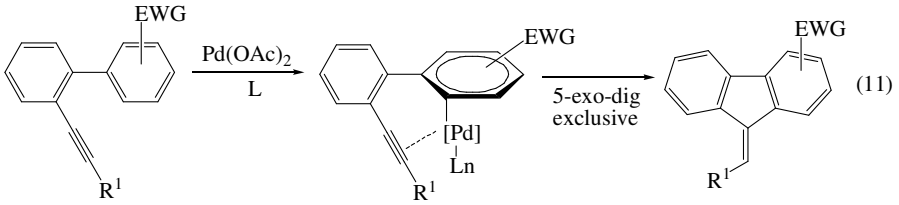
Scheme 9



(10)

The first example of the palladium-catalyzed exclusive 5-*exo-dig* hydroarylation of *o*-alkynyl biaryls has been demonstrated. This hydroarylation reaction efficiently proceeds with electron-neutral and electron-deficient arenes, producing fluorene frameworks with defined stereochemistry of the double bond (**Scheme 10**)[17].

Scheme 10

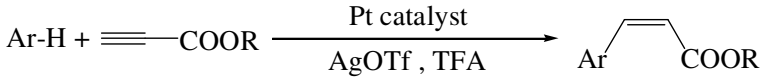


(11)

There has been reported that **$PtCl_2$/AgOAc** catalyzed the hydroarylation reaction under the same reaction conditions as **$Pd(OAc)_2$**[10k]. **Pt(II)** catalyst exhibits lower catalytic activity compared with **Pd(II)** catalyst, but better selectivity. The hydroarylation reaction of ethyl propiolates with arenes selectively forms ethyl cinnamates without the formation of diene (**Scheme 3**).

Kitamura *et al* reported that complexes **K_2PtCl_4/AgOTf** and **$PtCl_2$/AgOTf** catalyze the hydroarylation reaction of propiolic acids and propiolic acid derivatives with arenes and give predominantly (*Z*)-cinnamic acid derivatives in good to high yields without the formation of diene (**Scheme 11**)[18].

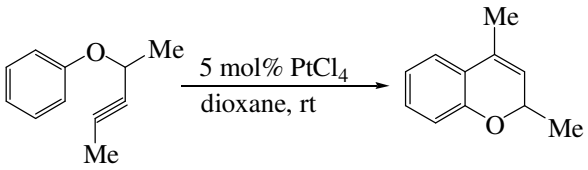
Scheme 11



(12)

Sames *et al* reported that **$PtCl_4$** catalyzed the intramolecular hydroarylation reaction of alkyne substrates, propargyl ethers and gave chromenes (**Scheme 12**)[19]. The reaction proceeds through the electrophilic aromatic substitution initiated by the coordination of **Pt** to the alkyne moiety.

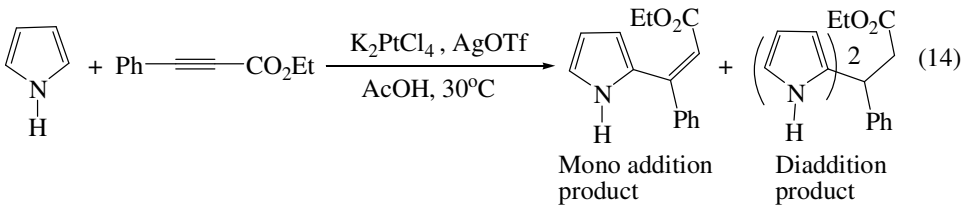
Scheme 12



(13)

Very recently, Kitamura *et al* reported that **K_2PtCl_4/AgOTf** catalyst system shows a drastic effect on the hydroarylation reaction of propiolic acid derivatives with pyrroles and furans. The hydroarylation reaction proceeds smoothly under mild conditions to give double hydroarylation products in good yields. Mono-adducts form only when the second hydroarylation reaction is inhibited by steric hindrance of substrates or low reactivity of the mono-adducts. The reaction of pyrroles with ethyl propiolates in the presence of **K_2PtCl_4/AgOTf** and AcOH solvent at 30°C affords a mixture of mono addition product, ethyl (2*Z*)-3(pyrrol-2-yl) cinnamate and a di-addition product, ethyl 3-phenyl-3,3-di(pyrrol-2-yl)propiolate (**Scheme 13**)[20]. Of these mixture of products, di-addition is the major product.

Scheme 13

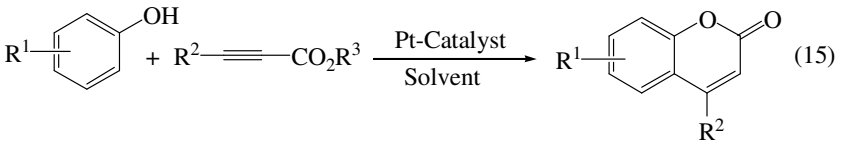


(14)

This hydroarylation reaction result is contrast to the **$Pd(OAc)_2$** reaction where only mono addition product was formed[11a]. This may be due to the fact that **K_2PtCl_4/AgOTf** is a more cationic and active catalyst than **$Pd(OAc)_2$**. This hydroarylation reaction can also be carried out using **$(^nNBu_4)_2PtCl_4$** in AcOH solvent even in the absence of the activating agent **AgOTf**.

Pt-catalysts such as **$PtCl_2$/AgOTf; K_2PtCl_4/AgOTf** and **K_2PtCl_4/AgOAc** can also be applied to the synthesis of coumarins through the intermolecular hydroarylation of propiolic acids with phenols (**Scheme14**)[21]. Propiolic acid reacts even with less reactive phenols in trifluoroacetic acid and affords coumarins and dihydrocoumarins. In the case of substituted propiolic acids, phenylpropiolic acid and 2-octynoic acid, the reaction proceeds selectively to afford coumarins in good to high yield.

Scheme 14

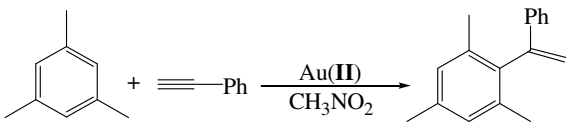


(15)

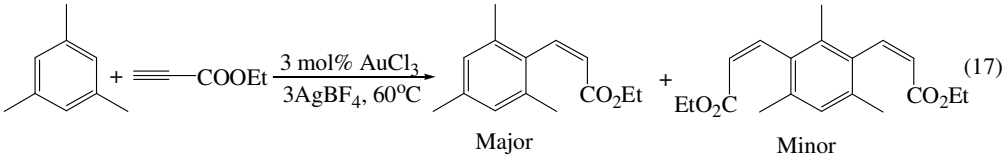
Reetz *et al* reported that **Au(I)** and **Au(III)** complexes catalyze the hydroarylation reaction of alkynes in the presence of the activating agents **AgOTf, $AgBF_4$, $AgSbF_6$** or **$BF_3.OEt_2$** (**Scheme 15**)[22]. In the case of terminal alkynes, complete regioselectivity in favor of the 1,1-disubstituted olefin is observed (Equiation 16 and **Scheme 15**). In the case of electron poor alkynes such as acetylene carboxylic acid ester, **Au(I)** complex such as **[Ph_3PAuCl]** activated by silver salts or **$BF_3.OEt_2$** is the best catalyst, resulting in opposite regioselectivity and high degree of (*Z*) selectivity (Equation 17 and **Scheme 15**).

The advantage of the gold-catalyzed hydroarylation reaction is that the gold-catalyzed hydroarylation reaction occurs under neutral conditions whereas, the **Pd** and **Pt-**catalyzed hydroarylation reactions occur in the presence of trifluoroacetic acid.

Scheme 15



(16)

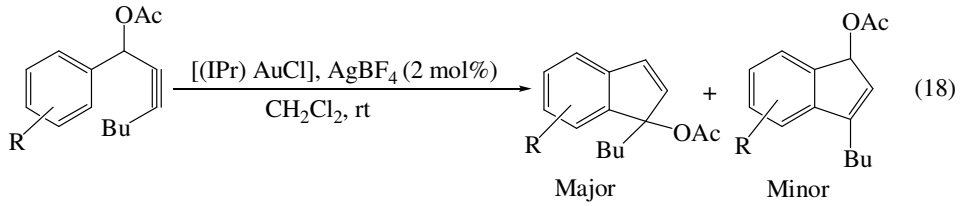


(17)

Hydroarylation reaction of alkynes can also be carried out using **$AuCl_3$/AgOTf** catalyst system[23]. Using this catalyst system electron deficient arenes can be efficiently functionalized with alkyne substrates. This reaction can be run with neat reactants at ambient temperature. Under the "**solvent-free**" conditions, a clean product forms from equimolar amounts of arene and alkyne substrates. **$AuCl_3$** also acts as an excellent catalyst to mediate the hydroarylation reaction of electron deficient alkenes and alkynes with various heterocycles under mild reaction conditions. This gold (**III**)-based method tolerates different functional groups such as aldehyde, carboxylic acid, and nitrile, and is highly efficient [24].

Steven *et al* reported that propargylic acetates undergo intramolecular hydroarylation reaction in the presence of cationic gold(**I**) complexe, **[(IPr)AuCl]** (IPr = N,N'-bis(2,6-diisopropylphenyl)imidazol-2-ylidene) and a silver salt, **$AgBF_4$** in CH_2Cl_2 solvent at room temperature and give indenes (**Scheme 16**)[25].

Scheme 16

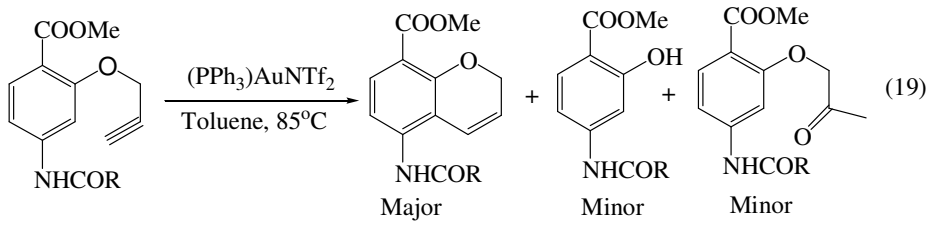


(18)

Triphenylphosphine gold (**I**) bis(trifluoromethanesulfonyl)imidate complex, **$(Ph_3P)AuNTf_2$** in toluene at 85°C also mediates the intramolecular hydroarylation

reaction and forms methyl-5-amino-2H-1-benzopyran-8-carboxylate derivatives (**Scheme 17**)[26].

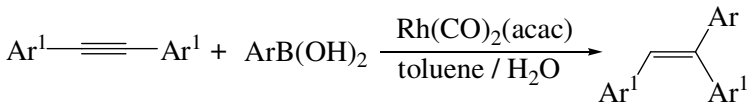
Scheme 17



(19)

$Rh(CO)_2(acac)$ is found to be an efficient and simple catalyst in the hydroarylation reaction of diarylacetylenes with boronic acid in the absence of phosphine ligand. Thus, triaryl-substituted olefins are prepared in good to excellent yields using this catalyst in the presence of toluene/H_2O. In dry toluene **$Rh(CO)_2(acac)$**(acac = acetylaceto) does not produce the desire product. No 1,4-rhodium shift is observed in the catalytic cycle (**Scheme 18**)[27].

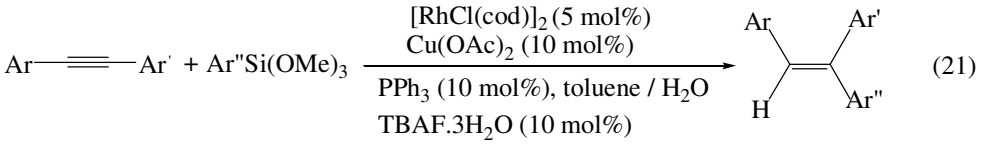
Scheme 18



(20)

Cheng *et al* reported that **rhodium-copper-TBAF-**mediates the hydroarylation reaction of alkynes with aryl trimethoxysilanes. The procedure utilizes a catalytic amount of copper (**II**) acetate, rhodium, **PPh_3** and **$TBAF{\cdot}3H_2O$** under air. The presence of an appropriate amount of water is crucial to the reaction. The reaction does not proceed in dry toluene, and an excess amount of water decreases the yield. Higher yield is obtained when the reaction is carried out under air instead of under nitrogen atmosphere. Thus, the rigorous exclusion of air/moisture is not required in this reaction to have the desire product and yield. Some asymmetric alkynes give the products with high regioselectivities (**Scheme 19**)[28].

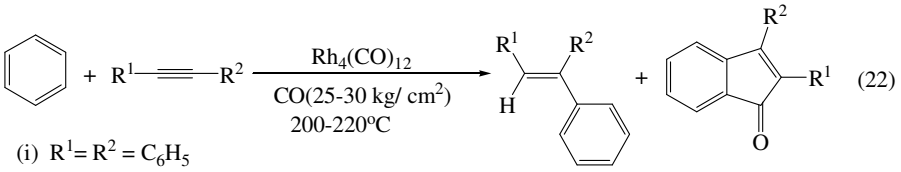
Scheme 19



(21)

Yamazaki *et al* reported that the complex, **$Rh_4(CO)_{12}$** acts as a catalyst in the hydroarylation reaction of internal alkynes, diphenylacetylene with benzene under the influence of heat and the pressure of carbon monoxide and affords triphenylethylene and 2,3-diphenylindenone (**Scheme 20**)[29]. The reaction of mono-/disubstituted benzenes with acetylene also gives the corresponding olefins and 2,3-diphenylindenones. High pressure of CO (25-30kg/cm^2) is important to have the good yield of the product triphenylethylene. Using high pressure such as 100kg/cm^2 forms other products whose structures are not determined yet.

Scheme 20



(22)

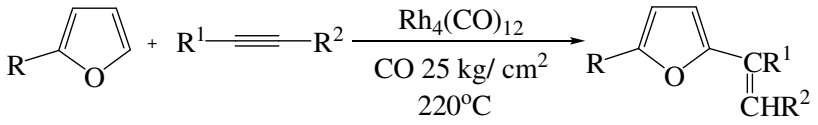
(i) $R^1 = R^2 = C_6H_5$

(ii) $R_1 = C_6H_5$, $R_2 = CH_3$

(iii) $R_1 = R_2 = p\text{-}CH_3C_6H_4$

$Rh_4(CO)_{12}$ also mediates the hydroarylation reaction of internal alkynes with heteroarene such as furan under the pressure of carbon monoxide and gives 1-(2-furyl)-1,2-diphenylethylene in a 80% yield (**Scheme 21**)[30]. Similarly, thiophene and *N*-methyl pyrrole react with alkynes to afford the corresponding olefins.

Scheme 21



(23)

(i) $R^1 = R^2 = C_6H_5$

(ii) $R_1 = C_6H_5$, $R_2 = CH_3$

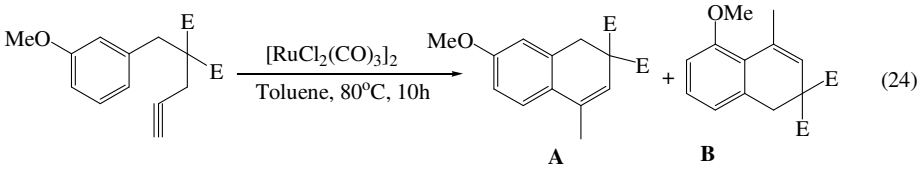
(iii) $R_1 = R_2 = p\text{-}CH_3C_6H_4$

R = H, CH_3, CH_3CO_2, CH_3CO and CHO

2-Phenylpyridine reacts with internal alkynes via **C-H** bond activation by a catalyst, **$RhCl(PPh_3)_3$**, to give the *ortho* alkenylated products[31].

The **Ru**-complex, **$[RuCl_2(CO)_3]_2$** catalyzed the intramolecular hydroarylation reaction of aryl-1-alkynes in toluene under the influence of heat[32]. The reaction of diethyl(*m*-methoxybenzyl)(propargyl)malonate with 4 mol% of **$[RuCl_2(CO)_3]_2$** in toluene at 80°C for 10h resulted in cyclization to the six membered dihydronaphthalene derivatives **A** and **B** in 81% yield in a ratio of 93:7(**Scheme 22**). **$PtCl_2$** also showed a high catalytic activity (76% yield with 99:1 for 7hrs). The use of **AgOTf** as an additive enhances the reactivity of the catalyst. In the presence of 8 mol% of **$[RuCl_2(CO)_3]_2$** and 16 mol% of **AgOTf** the reaction completes within 0.5h and gives a 78:22 mixture of the products **A** and **B** in a total yield of 86%. This result apparently shows that the addition of **AgOTf** renders the catalyst more electrophilic and less selective.

Scheme 22

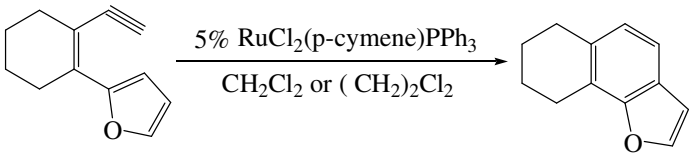


(24)

Merlic *et al*, on the other hand, reported that the **Ru**-complexes such as **$RuCl_2(C_6H_6)PPh_3$**, **$RuCl_2$(*p*-cymene)PPh_3**, **$RuCl_2(C_6H_6)[P(OEt)_3]$**, and **$RuCl_2(C_6H_6)AsPh_3$** catalyze the intramolecular hydroarylation reaction of dienyl

alkynes (**Scheme 23**)[33]. Among these **Ru**-complexes, **$RuCl_2$(*p*-cymene)PPh_3** is the most efficient catalyst for the cyclization of dienylalkynes.

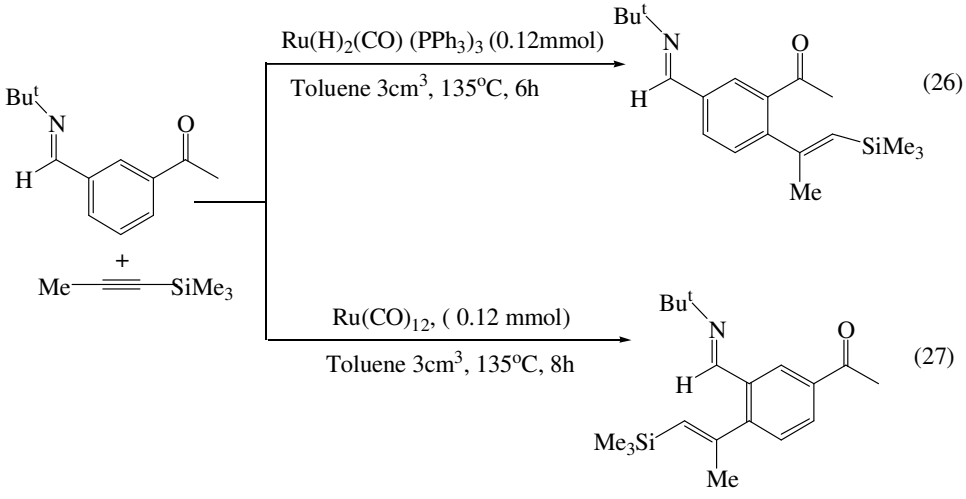
Scheme 23



(25)

Recently, two **Ru**-complexes, such as **$Ru(H)_2(CO)(PPh_3)_3$** and **$Ru_3(CO)_{12}$** have been discovered that they allow for the production of two different products, which are individually selective from the same combination of reactants by changing the catalyst. In this new **C-H**/olefin coupling reaction of aromatic compounds having both keto and imino substituents, the site of the **C-H** bond to be cleaved is catalyst specific (**Scheme 24**)[34]. When the complex, **$Ru(H)_2(CO)(PPh_3)_3$** is used as a catalyst, the **carbon-carbon** bond formation takes place at the position *ortho* to the acetyl group (Equation 26 and **Scheme 24**). On the other hand, in the presence of the complex, **$Ru_3(CO)_{12}$** the **carbon-carbon** bond formation takes place at the position *ortho* to the imino group (Equation 27 and **Scheme 24**). It may be noted that the starting materials and the reaction conditions for these two reactions are essentially identical.

Scheme 24

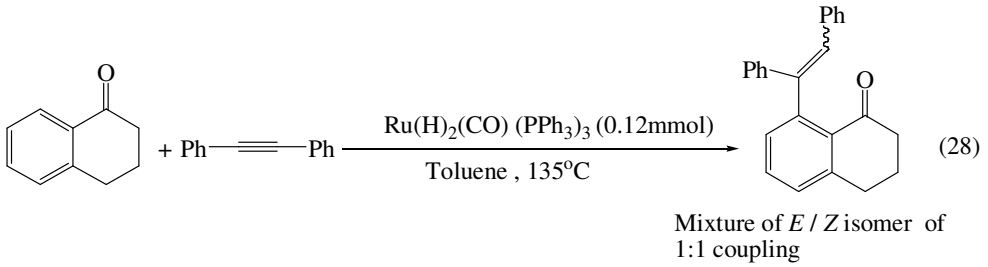


(26)

(27)

The reaction of α-tetralone with various internal alkynes in the presence of **Ru-**complex, **$Ru(H)_2(CO)(PPh_3)_3$** gives 1:1 addition products (**Scheme 25**)[35]. Symmetrically substituted dialkyl and diaryl acetylenes give *E*/*Z* mixture of 1:1 coupling products in good yields. The addition is highly *cis*-selective.

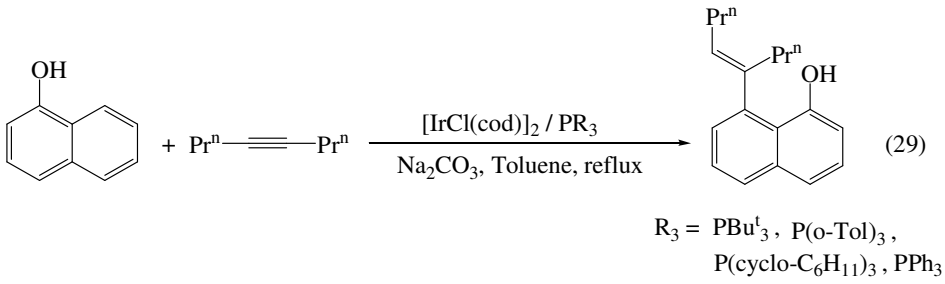
Scheme 25



Ruthenium-catalyzed coupling reaction of aromatic ketones with alkynylsilanes gives in most cases *ortho* vinylation adducts in high yield. The predominant stereochemistry of the newly introduced double bond is *E*. In contrast, 1-acetylnaphthalene undergoes a one pot insertion cyclization reaction[36].

1-Naphthol effectively couples with internal alkynes in the presence of an iridium complex, **$[IrCl(cod)]_2$** to afford the corresponding 8-substituted 1-naphthol derivatives selectively **(Scheme 26)**[37]**.**

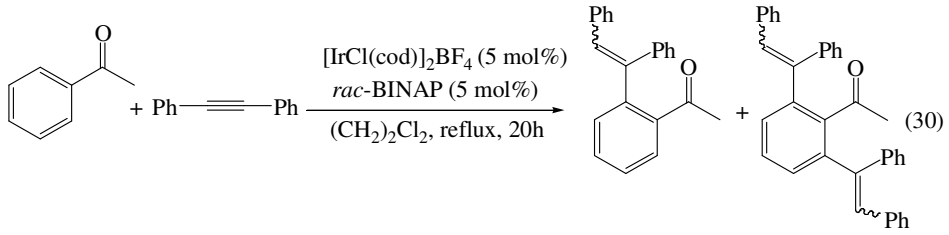
Scheme 26



Shibata *et al* reported that cationic **Ir-**complex, **$([Ir(cod)_2]BF_4$ + BINAP)** catalyzed the addition of *ortho*-**C-H** bond of aryl ketones to alkynes, which gave alkenylated products in good to high yields (**Scheme 27**)[38]. In this reaction the **carbon-carbon** bond formation takes place at the position *ortho* to the carbonyl

group, that is, in the present reaction involves the carbonyl directed *ortho*- **C-H** bond cleavage of aryl ketones and *syn*-addition to diphenylacetylene.

Scheme 27



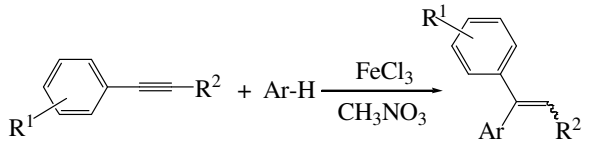
(30)

Bis(1,5-cyclooctadiene)nickel is found to be an effective catalyst for the addition of aryl groups of arylboron compounds to alkynes in the presence of a proton source, which gives various polysubstituted alkenylarenes or dienylarenes selectively[39].

Hiyama *et al* reported that nickel complexes having a bulky tri(sec-alkyl)phosphine ligand catalyze the hydroheteroarylation of alkynes at 35°C. Selective activation of an **Ar-H** bond over an **Ar-CN** bond of N-protected 3-cyanoindole is achieved by a proper choice of ligand and/or an N-protecting group. The catalyst is applicable to a diverse range of heteroarenes to afford *cis*-hydroheteroarylation products in high chemo-and stereoselective manners[40].

Aryl-substituted alkynes undergo hydroarylation reaction with electron rich arenes smoothly in the presence of **$FeCl_3$** in CH_3NO_3 solvent under mild conditions (**Scheme 28**)[41].

Scheme 28



(31)

R^1 = H, *m*-OMe, *p* -OMe, *p* -Cl,
2,4,5-trimethyl, n-pentyl.

R^2 = H, Me, COOEt, Ph.

1.2.2. Metal- free hydroarylation of alkynes

Literature survey reveals that till now, the formation of **carbon-carbon** bond through the hydroarylation reaction of alkynes under metal-free conditions has not attracted the attention of the chemists.

1.3. Aim of the Present Research works

No doubt the reported metal-catalyzed hydroarylation reactions so far discussed are excellent, efficient and powerful synthetic methods for the direct formation of new **carbon-carbon** bond between arenes and alkynes. But still there are some limitations, such as to carry out a transition metal-catalyzed hydroarylation reaction requires high temperature, strong acidic conditions and special cautions for handling metal catalysts under inert atmosphere. Furthermore, contamination of pharmaceutical materials with a trace amount of metals in the processes of manufacture causes a serious problem. Besides these, literature survey reveals that in most cases the reported transition metals alone can not act as an efficient catalyst. An appropriate activating agent is required to improve the catalytic activity of the transition metals. In many cases more than one activating agents and more than equimolar amounts of activating agents are required to improve the catalytic activity of the reported transition metals. Thus a lot of hazardous salty waste products formed during the reactions that may be the cause of the pollution of the environment. Some transition metals and some catalyst activating agents are very expensive that not only increase the reagent cost but also increase the production cost.

Similar situations arise in the case of the iodoarylation reaction of alkynes as well as in the direct iodination of aromatic compounds using molecular iodine because molecular iodine alone is not a powerful electrophile. Therefore, to carry out the iodoarylation reaction of alkynes and to carry out the direct iodination reaction of aromatic compounds using molecular iodine require an appropriate oxidizing agent to convert molecular iodine into a powerful electrophile. In order to prevent the environment pollution and to reduce the production cost, organic chemists are seeking to develop a new, clean, environmentally friendly and milder synthetic method for the direct formation of **carbon-carbon** bond between arenes and

alkynes and for the direct iodination of aromatic compounds, without the involvement of **toxic** transition metals. The recent demand for highly efficient, cheap, clean and environmentally benign syntheses of fine chemicals and pharmaceutical products has encouraged the author to develop a mild, cheap and simple synthetic method for the direct formation of **carbon-carbon** bond between arenes and alkynes, and for the direct iodination of aromatic compounds.

In this dissertation, the present research work has been concentrated on the development of efficient, simple, cheap and effective synthetic method for the direct formation of **carbon-carbon** bond between arenes and alkynes, and for the direct iodination of aromatic compounds without the involvement of **toxic** transition metals.

In this dissertation the author has developed four simple, cheap, effective, environmentally benign and very efficient synthetic methods for the direct formation of new **carbon-carbon** bond between arenes and alkynes using (**i**) **$FeCl_3$/AgOTf** catalyst system in the presence of trifluoroacetic acid **(ii) BF_3** catalyst (**iii**) only trifluoroacetic acid, and (**iv**) molecular iodine in the presence of hypervalent iodine reagents, without the involvement of toxic transition metals. The author has also established a very simple, effective and efficient synthetic method for the direct iodination of aromatic compounds using molecular iodine in the presence of potassium peroxodisulfate in TFA and H_2SO_4. Results of these developed synthetic methods are discussed in the **chapter 2**, **3, 4**, **5** and **6** of the dissertation**.**

Chapter 2 describes an effective, very simple, environmentally benign and efficient **$FeCl_3$/AgOTf** mediated hydroarylation reaction of arylsubstituted alkynes for the direct formation of new **carbon-carbon** bond between arenes and alkynes.

Chapter 3 describes an effective, very simple **BF_3** mediated hydroarylation reaction of arylsubstituted alkynes for the direct formation of new **carbon-carbon** bond between arenes and alkynes.

Chapter 4 describes an effective, very simple, cheap, environmentally benign and efficient trifluoroacetic acid mediated hydroarylation reaction of arylsubstituted alkynes for the direct formation of new **carbon-carbon** bond between arenes and alkynes without the involvement of transition metals.

Chapter 5 describes an effective, very simple, cheap, environmentally benign and efficient synthetic method for the direct formation of new **carbon-carbon** bond between electron rich arenes and arylsubstituted alkynes through the iodoarylation reaction using molecular iodine in the presence of hypervalent iodine reagents in acetonitrile solvent without the involvement of transition metals.

Chapter 6 describes an effective, simple, cheap and efficient synthetic method for the direct periodination of aromatic compounds, and for the direct preparation of selective aromatic diiodo compounds using molecular iodine in the presence of potassium peroxodisulfate in TFA, H_2SO_4 and dicloroethane solvent.

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CHAPTER 2

$FeCl_3$/AgOTf Catalyzed Hydroarylation of Alkynes

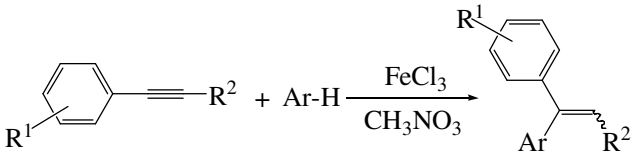
A Very Convenient, Simple Procedure for Substituted Arylalkenes from Simple Arenes

2.1. Introduction

Iron is a group **8** and period **4** element in the periodic table and is therefore, classified as a transition metal (**[Ar]4s^{2}3d^6**). Iron is a cheap, readily available, non-toxic and environmentally friendly transition metal which shows increasing and promissing catalytic ability in many organic syntheses[1].

Very recently Lu *et al* reported the hydroarylation reaction of arylsubstituted alkynes with simple and substituted arenes in the presence of **$FeCl_3$** in CH_3NO_3 solvent without using any additives under mild conditions (**Scheme 1**)[2]. Aryl-substituted alkynes undergo hydroarylation reaction with electron rich arenes smoothly to afford 1,1-diarylalkenes.

Scheme 1



(1)

R^1 = H, *m*-OMe, *p* -OMe, *p* -Cl,
2,4,5-trimethyl, n-pentyl.
R^2 = H, Me, COOEt, Ph.

To improve the catalytic activity of **$FeCl_3$** it is necessary to increase the cationic property of **$FeCl_3$** because the hydroarylation reaction of olefins are considered to proceed through the electrophilic aromatic substitution. Silver triflate, **AgOTf** is thought to undergo ligand exchange reaction with **$FeCl_3$** and forms more cationic and more effective **$Fe(OTf)_3$** species.

In this chapter, a more convenient and very simple **carbon-carbon** bond formation method between electron rich arenes and aryl substituted alkynes using **$FeCl_3$/AgOTf** catalyst system in the presence of trifluoroacetic acid and dichloromethane solvent is reported.

2.2. Results and Discussion

2.2.1. *Optimization of the reaction conditions*

Direct preparation of 1,1-diarylalkenes was carried out from the corresponding arenes and alkynes using **$FeCl_3$ /AgOTf** catalyst system in the presence of trifluoroacetic acid and CH_2Cl_2 solvents at 30°C. In the present study, to have an effective catalyst system and to optimize the reaction conditions initially, the work was confined on the efficiency of the hydroarylation reaction of phenylacetylene **1** with benzene **2j** in the presence of different combinations of **$FeCl_3$** catalyst, additives and solvent systems under different reaction conditions (**Scheme 2**). The results are given in **Table 1**.

Scheme 2. Hydroarylation reaction of phenylacetylene **1** with benzene **2j** in the presence of different combinations of **$FeCl_3$** catalyst, additives and solvent systems under different reaction conditions.

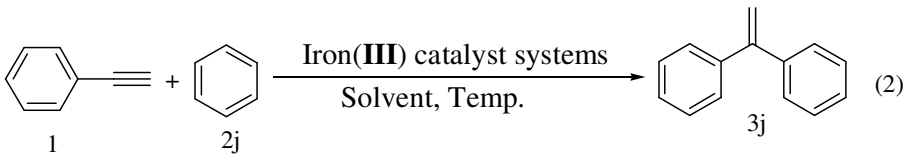


Table 1. Hydroarylation reaction of phenylacetylene **1** with benzene **2j** in the presence of different combinations of **$FeCl_3$** catalyst, additives and solvent systems under different reaction conditions[a].

Entry	Catalyst	Temp(°C)	Time(h)	Product	Yield(%)[b]
1	$FeCl_3$ /TFA	30	72	No product	-[c]
2	$FeCl_3$ /AgOTf	30	72	3j	10[d]
3	$FeCl_3$/AgOTf /TFA	30	60	3j	18[e]
4	$FeCl_3$ /AgOTf /TFA	30	60	3j	14[f]
5	$FeCl_3$ /AgOTf /TFA	45	60	3j	17[g]
6	$FeCl_3$	30	60	No product	-[h]
7	$FeCl_3$ /AgOTf	30	60	No product	-[i]

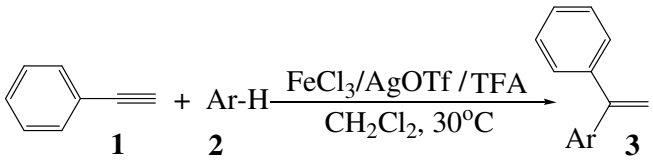
[a]***Reaction conditions*** : Benzene **2j** (100.0 mmol), phenylacetylene **1**(1.0 mmol), CH_2Cl_2 (1.0 mL), molecular sieve 4A (3-4 pieces, 0.20 ~ 0.25g).
[b]Isolated yield based on phenylacetylene **1**.
[c]$FeCl_3$ (0.10 mmol), TFA (1.0 mL).
[d]$FeCl_3$ (0.10 mmol), AgOTf (0.30 mmol).
[e]$FeCl_3$ (0.10 mmol), AgOTf (0.30 mmol), TFA (1.0 mL).
[f]$FeCl_3$ (0.20 mmol), AgOTf (0.60 mmol), TFA (1.0 mL).
[g]$FeCl_3$ (0.10 mmol), AgOTf (0.30 mmol), TFA (1.0 mL), $(CH_2)_2Cl_2$ (1.0 mL).
[h]$FeCl_3$ (0.10 mmol).
[i]$FeCl_3$ (0.10 mmol), AgOTf (0.30 mmol), CH_3NO_3 (1.0 mL).

The reaction using **$FeCl_3$/AgOTf** catalyst system in the presence of TFA at 30°C for 60 hours afforded the hydroarylation product **3j** in 18% yield (Entry 3). Increasing the amount of **$FeCl_3$** and **AgOTf** did not improve the yield (Entry 4). No hydroarylation reaction occured in the presence of the catalyst systems **$FeCl_3$/TFA** and only in the presence of **$FeCl_3$** (Entries 1 and 6). Furthermore, elevation of the reaction temperature did not improve the yield (Entry 5). When the reaction was carried out using **$FeCl_3$/AgOTf** catalyst system without TFA the hydroarylation product **3j** was formed in 10% yield in the presence of CH_2Cl_2 solvent (Entry 2), but use of nitromethane solvent did not form any hydroarylation product (Entry 7). From the above screening results it was found that the entry 3 is the optimum condition for the reaction.

2.2.2. *Scope of the hydroarylation reaction*

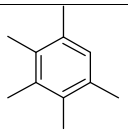
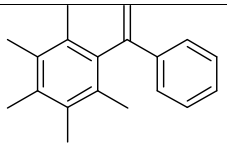
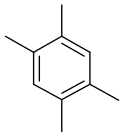
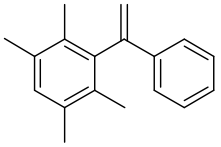
Using the reaction conditions of the entry 3 the hydroarylation reaction of phenylacetylene **1** was conducted with different electron rich arenes **2** **(Scheme 3)**. The results are given in **Table 2.**

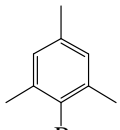
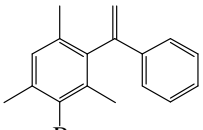
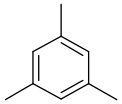
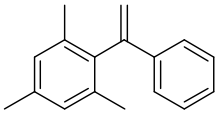
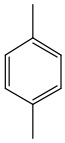
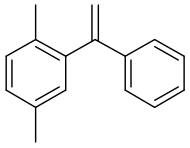
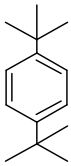
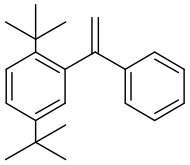
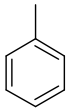
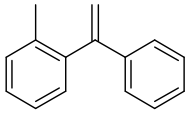
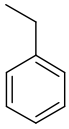
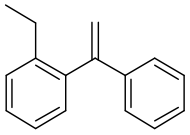
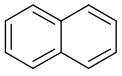
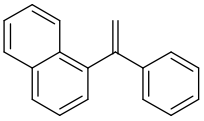
Scheme 3. Hydroarylation reaction of phenylacetylene **1** with different electron rich arenes **2** in the presence of **$FeCl_3$/AgOTf** catalyst system.



(3)

Table 2. Hydroarylation reaction of phenylacetylene **1** with different electron rich arenes **2** in the presence of **$FeCl_3$/AgOTf** catalyst system[a].

Entry	Arene 2	Time(h)	Product 3	Yield (%)[b]
1	 2a	30	 3a	77
2	 2b	24	 3b	80

3		2c	56		3c	62
4		2d	24		3d	86[c]
5		2e	24		3e	50
6		2f	60		3f	15
7		2g	60		3g	27
8	2g		60	3g		17[d]
9		2h	60		3h	9[e]
10		2i	60		3i	18

[a]***Reaction conditions***: Arene **2** (5.0 mmol), phenylacetylene **1** (1.0 mmol), $FeCl_3$ (0.10 mmol), AgOTf (0.30 mmol), TFA (1.0 mL), CH_2Cl_2 (3.0 mL), molecular sieve 4A(3-4 pieces, 0.20~0.25g) at 30°C.

[b]Isolated yield based on phenylacetylene **1**.

[c]CH_2Cl_2 (6.0 mL) was used

[d]Reaction was carried out in the absence of molecular sieve.

[e]10.0 mmol of arene was used.

The reaction of electron rich arenes **2** such as pentamethylbenzene **2a**, 1,2,4,5-tetramethylbenzene **2b**, 1-bromo-2,4,6-trimethylbenzene **2c**, 1,3,5-trimethylbenzene **2d**, and 1,4-dimethylbenzene **2e** afforded 1-aryl-1-phenylethenes **3** in good to high yields (Entries 1-5). The sterically bulky 1,4-di-

tert-butylbenzene **2f** showed very low reactivity with phenylacetylene **1** and afforded the hydroarylation product **3f** in 15% yield (Entry 6). Toluene **2g** and ethylbenzene **2h,** on the other hand, reacted with phenylacetylene **1** under the same reaction conditions and gave selectively *ortho*-hydroarylation product **3g** and **3h** in 27 and 9% yields (Entries 7 and 9), respectively.

Naphthalene **2i** also showed a low reactivity with phenylacetylene **1** and gave 1,1-diarylethene **3i** in 18% yield (Entry 10).

Next, the hydroarylation reactions of 4-methylphenylacetylene **4**, with different electron rich arenes **2** was carried out under the same reaction conditions (**Scheme 4**) as that of the reaction of phenylacetylene **1** with different arenes **2**. The results are given in **Table 3.** In the reaction of 4-methylphenylacetylene **4** with electron rich arenes **2a-2d,** excellent yields of the hydroarylation products **5** were obtained (Entries 1-4). However, the reaction with *p*-xylene **2e** resulted in a low yield of the product **5e** (Entry 5).

Scheme 4. Hydroarylation reaction of 4-methylphenylacetylene **4** with different electron rich arenes **2** in the presence of **$FeCl_3$/AgOTf** catalyst system.

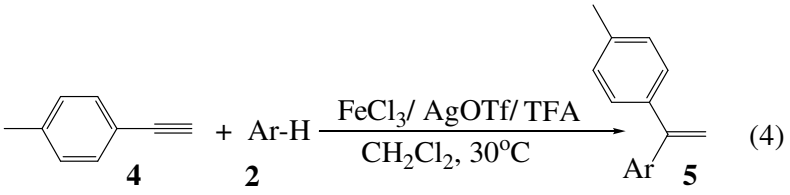
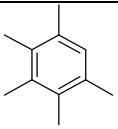
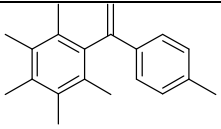
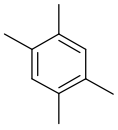
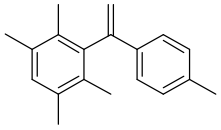
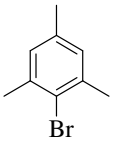
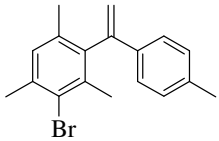
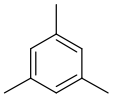
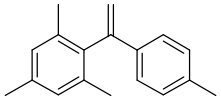
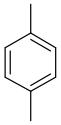
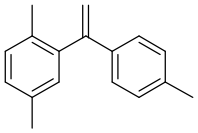


Table 3. Hydroarylation reaction of 4-methylphenylacetylene **4** with different electron rich arenes **2** in the presence of **$FeCl_3$/AgOTf** catalyst system[a].

Entry	Arene 2	Time(h)	Product **5**	Yield (%)[b]
1	 2a	30	 5a	78
2	 2b	24	 5b	84

3	 2c	60	 5c	63
4	 2d	24	 5d	81
5	 2e	24	 5e	09

[a]***Reaction conditions:*** Arene **2** (5.0 mmol), 4-methylphenylacetylene **4** (1.0 mmol), $FeCl_3$ (0.10 mmol), AgOTf (0.30 mmol), TFA (1.0 mL), CH_2Cl_2 (3.0 mL), molecular sieve 4A (3-4 pieces, 0.20~0.25g) at 30°C.

[b]Isolated yield based on 4-methylphenylacetylene **4.**

Again, the reaction of an electron withdrawing group containing alkyne, 4-fluorophenylacetylene **6** was examined with various electron rich arenes **2** under the above reaction conditions (**Scheme 5**). The results of the reactions are shown in **Table 4**. The reaction of electron rich arenes **2a-2d** gave the hydroarylation products **7** in good yields (Entries 1-4). The moderately electron rich arenes such as *p*-xylene **2e** showed moderate type of reactivity with 4-fluorophenylacetylene **6** and the yield was 55% (Entry 5).

Scheme 5. Hydroarylation reaction of 4-fluorophenylacetylene **6** with different electron rich arenes **2** in the presence of **$FeCl_3$/AgOTf** catalyst system.

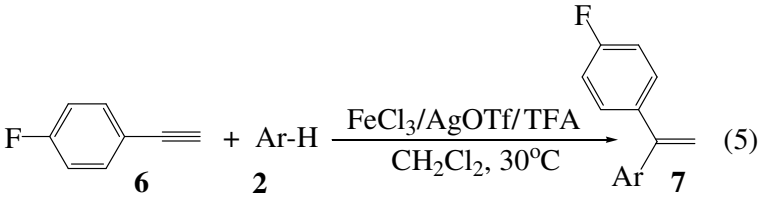
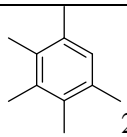
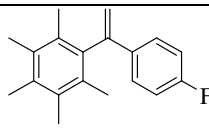
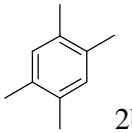
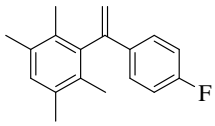
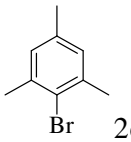
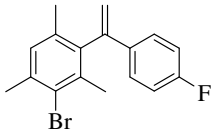
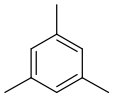
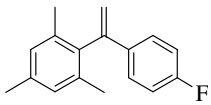
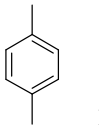
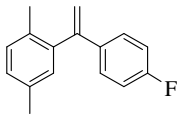


Table 4. Hydroarylation reaction of 4-fluorophenylacetylene **6** with different electron rich arenes **2** in the presence of **$FeCl_3$/AgOTf** catalyst system[a].

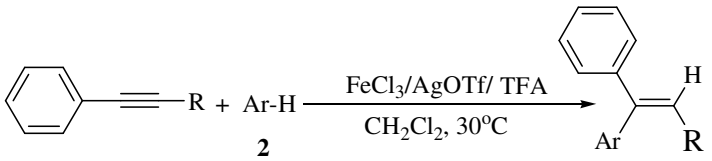
Entry	Arene 2	Time(h)	Product 7	Yield (%)[b]
1	 2a	30	 7a	70
2	 2b	24	 7b	66
3	 2c	60	 7c	60
4	 2d	24	 7d	71
5	 2e	24	 7e	55

[a]***Reaction conditions***: Arene **2** (5.0 mmol), 4-fluorophenylacetylene **6** (1.0 mmol), $FeCl_3$ (0.10 mmol), AgOTf (0.30 mmol), TFA (1.0 mL), CH_2Cl_2 (3.0 mL), molecular sieve 4A (3-4 pieces, 0.20~0.25g) at 30°C.

[b]Isolated yield based on 4-fluorophenylacetylene **6.**

Finally, the reactions of internal alkyne diphenylacetylene **8** and 1-methyl-2-phenylacetylene **9** were examined with various electron rich arenes **2** under the above reaction conditions (**Scheme 6**). The results of the reactions are shown in **Table 5**. The reaction of diphenylacetylene **8** with pentamethylbenzene **2a** gave the hydroarylation product **10a** in moderate yield (Entry 1). On the other hand, the reactions of 1-methyl-2-phenylacetylene **9** with pentamethylbenzene **2a,** 1,2,4,5-tetramethylbenzene **2b**, 1-bromo-2,4,6-trimethylbenzene **2c**, 1,3,5-trimethylbenzene **2d**, and 1,4-dimethylbenzene **2e** afforded 1-aryl-1-phenylethenes **11** in moderate to good yields (Entries 2-6).

Scheme 6. Hydroarylation reaction of internal alkynes **8** and **9** with different electron rich arenes **2** in the presence of **$FeCl_3$/AgOTf** catalyst system.

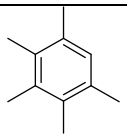
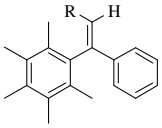
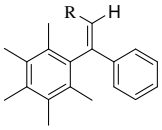
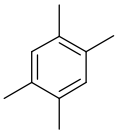
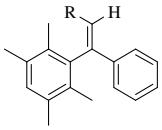
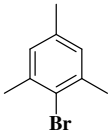
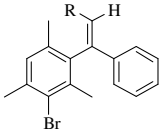
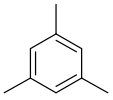
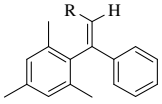
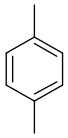
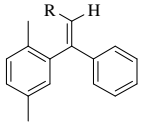


(6)

8. R = Ph
9. R = CH_3

10. R = Ph
11. R = CH_3

Table 5. Hydroarylation reaction of internal alkynes **8** and **9** with different electron rich arenes **2** in the presence of **$FeCl_3$/AgOTf** catalyst system[a].

Entry	Arene 2	Alkyne	Time(h)	Product	Yield (%)[b]
1	 2a	8	48	 10a	54
2	2a	9	48	 11a	67
3	 2b	9	36	 11b	62
4	 2c	9	60	 11c	49
5	 2d	9	36	 11d	66
6	 2e	9	36	 11e	62

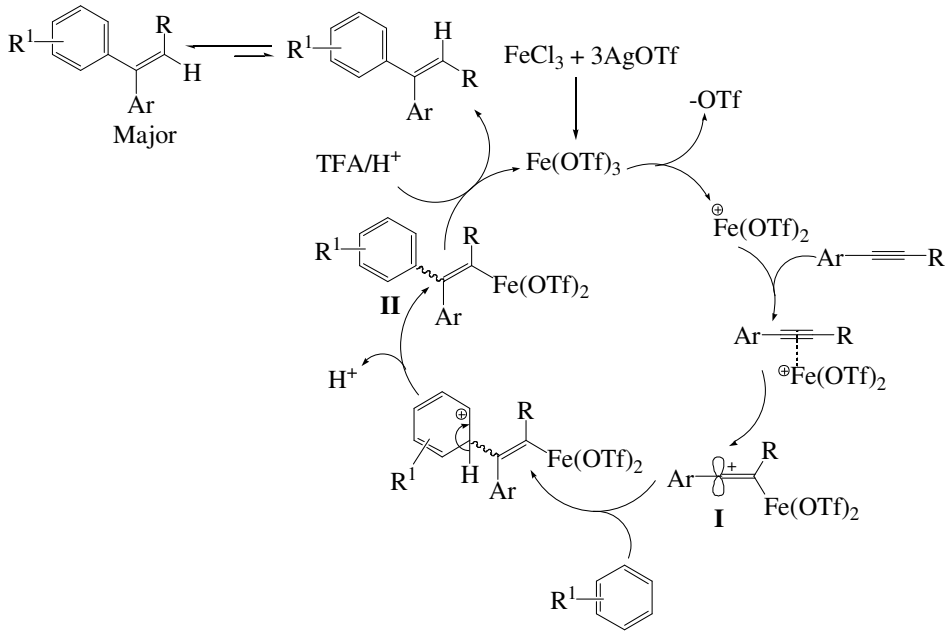
[a]***Reaction conditions***: Arene **2** (5.0 mmol), alkynes **8** and **9** (1.0 mmol), $FeCl_3$ (0.10 mmol), AgOTf (0.30 mmol), TFA (1.0 mL), CH_2Cl_2 (3.0 mL), molecular sieve 4A (3-4 pieces, 0.20~0.25g) at 30°C.

[b]Isolated yield based on alkynes **8** and **9.**

2.2.3. *Possible mechanism of the $FeCl_3$/AgOTf catalyzed hydroarylation reaction*[2]

The hydroarylation reaction between arenes and arylsubstituted alkynes in the presence of **$FeCl_3$/AgOTf** catalyst system is considered to be a Friedel-Crafts type reaction (**Scheme 7**). First of all, **$FeCl_3$** reacts with **AgOTf** and forms a more cationic species **$Fe(OTf)_3$**. The resulting cationic **$Fe(OTf)_3$** species attacks to the aryl-substituted alkynes and forms a more stable alkenyl cation **I**. The alkenyl cation **I** then undergoes electrophilic aromatic substitution reaction with arenes and forms the intermediate **II** in excellent regioselectivity. Finally, the intermediate **II** undergoes protonation and isomerization to form the desire 1,1-diarylalkene and complete the catalyst cycle.

Scheme 7. Mechanism of the $FeCl_3$/AgOTf catalyzed hydroarylation reaction of alkynes



In summary, the author has demonstrated that the **$FeCl_3$/AgOTf** catalyzed hydroarylation reaction of alkynes proceeds smoothly and efficiently in the presence of trifluoroacetic acid (TFA) when arylsubstituted alkynes and electron rich arenes are used. The simplicity of this procedure along with the mildness is practical as a synthetic tool of arylalkenes. In the case of toluene and ethyl benzene selectively form *ortho*-hydroarylation products.

2.3. Experimental Section

General

All solvents and starting materials were used during the research works as received without further purification unless otherwise indicated. ^{1}H NMR and ^{13}C NMR were recorded on a JEOL JNM-Al-300FT-NMR spectrometer in $CDCl_3$ solution (TMS as an internal standard). Melting points of the pure compounds were recorded by thin disc method on a YANACO electrothermal melting point apparatus and are uncorrected. Elemental analysis was performed by the Service Center of the Elemental Analysis of Organic Compounds, Faculty of Science, Kyushu University, Fukuoka, Japan.

General procedure for the hydroarylation of alkynes

Required amounts of **$FeCl_3$** (0.10 mmol), **AgOTf** (0.30 mmol), TFA(1.0 mL), CH_2Cl_2 (3.0 mL) and molecular sieve 4A (3-4 pieces, 0.20~0.25g) were taken in a 25.0 mL quick-fit round bottom flask and stirred for about 15 minutes at room temperature. Arene (5.0 mmol), alkyne (1.0 mmol) and CH_2Cl_2 (2.0 mL) were then added into the catalysts mixture and stirred at 30^{o}C until the completion of the reaction. The reaction mixture was dissolved in 20 mL of dichloromethane and passed through a short path silica gel (~2.0g) column to remove the catalyst and molecular sieve. The product was eluted with dichloromethane and the collected dichloromethane was washed with 5% aqueous $NaHCO_3$ solution to remove the unreacted TFA and dried over anhydrous Na_2SO_4. Finally, dichloromethane was evaporated under reduced pressure below 40^0 **C.** Individual pure compounds were isolated from the reaction mixture by column chromatography using silica gel as a stationary phase.

***1-(Pentamethylphenyl)-1-phenylethene* 3a**[3]

Yield: 0.2162g (77%); white crystalline solid, Mp 71.4-72.7^{o}C.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.29-7.23(m, 5H, Ar-H), 5.97(d, 1H, vinyl-H, *J* =1.5Hz), 5.06(d, 1H, vinyl-H, *J* =1.2Hz), 2.29(s, 3H, Me), 2.24(s, 6H, 2xMe), 2.10(s, 6H, 2xMe).

^{13}C NMR (75 MHz, $CDCl_3$): δ =148.66, 140.03, 138.72, 133.70, 132.33, 131.56, 128.35, 127.41, 126.01, 114.27, 17.83, 16.75, 16.55.

***1-Phenyl-(2,3,5,6-tetramethylphenyl)ethene* 3b**[3]

Yield: 0. 1959g (80%); white crystalline solid, Mp 67.8-68.9°C.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.19-7.11(m, 5H, Ar-H), 6.88(s, 1H, Ar-H), 5.89 (d, 1H, vinyl-H, *J* =1.5Hz), 4.97(d, 1H, vinyl-H, *J* =1.5Hz), 2.16(s, 6H, 2xMe), 1.96(s, 6H, 2xMe).

^{13}C NMR (75 MHz, $CDCl_3$): δ =148.05, 141.08, 139.77, 133.51, 131.96, 130.29, 128.36, 127.47, 125.94, 114.16, 20.12, 16.63.

***1-(3-Bromo-2,4,6-trimethylphenyl)-1-phenylethene* 3c**[3]

Yield: 0.2093g (62%); colorless liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.30-7.24(m, H, Ar-H), 7.00(s, 1H, Ar-H), 5.97(d, 1H, vinyl-H, *J* =1.2Hz), 5.07(d, 1H, vinyl-H, *J* =1.5Hz), 2.42(s, 3H, Me), 2.27(s, 3H, Me), 2.07(s, 3H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ =147.07, 139.97, 138.97, 136.82, 136.13, 134.91, 129.61, 128.50, 127.78, 125.81, 125.45, 114.80, 23.94, 21.41, 19.91.

***1-Phenyl-1-(2,4,6-trimethylphenyl)ethene* 3d**[3]

Yield: 0.2252g (86%); colorless liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.27-7.20(m, 5H, Ar-H), 6.90(s, 2H, Ar-H), 5.95(d, 1H, vinyl-H, *J* =1.2Hz), 5.09(d, 1H, vinyl-H, *J* =1.2Hz), 2.31(s, 3H, Me), 2.11(s, 6H, 2xMe).

^{13}C NMR (75 MHz, $CDCl_3$): δ =146.91, 139.55, 138.17, 136.38, 136.08, 128.39, 128.11, 127.51, 125.82, 114.45, 21.02, 20.06.

***1-(2,5-Dimethylphenyl)-1-phenylethene* 3e**[3]

Yield: 0.1074g (50%); colorless liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.28-7.22(m, 5H, Ar-H), 7.06(m, 2H, Ar-H), 7.03(m,1H, Ar-H), 5.75(d, 1H, vinyl-H, *J* =1.2Hz), 5.18(d, 1H, vinyl-H, *J* =1.2Hz), 2.33(s, 3H, Me), 2.01(s, 3H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ =149.58, 141.46, 140.67, 135.02, 132.92, 130.65, 129.94, 128.28, 128.16, 127.49, 126.48, 114.61, 20.89, 19.57.

***1-(2,5-Di-tert-butylphenyl)-1-phenylethene* 3f**[3]

Yield: 0. 0481g (15%); white crystalline solid, Mp 74.8-76.3°C.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.44(d, 1H, Ar-H, *J* =8.4Hz), 7.32(d, 1H, Ar-H, *J* =2.1Hz), 7.05(d, 1H, Ar-H, *J* =2.4Hz), 7.29-7.23(m, 5H, Ar-H), 5.89(d, 1H, vinyl-H, *J* =1.2Hz), 5.22(d, 1H, vinyl-H, *J* =1.5Hz), 1.32(s, 9H, t-Bu), 1.22(s, 9H, t-Bu).
^{13}C NMR (75 MHz, $CDCl_3$): δ =151.69, 147.79, 144.80, 141.58, 139.64, 130.24, 128.16, 127.31, 126.89, 126.48, 123.98, 114.92, 36.19, 34.05, 32.26, 31.31.

***1-(2-methylphenyl)-1-phenylethene* 3g**[3]

Yield: 0.0583g (27%); colorless liquid.
^{1}H NMR (300 MHz, $CDCl_3$): δ =7.20-7.13(m, 9H, Ar-H), 5.69(d, 1H, vinyl-H, *J* =1.5 Hz), 5.11(d, 1H, vinyl-H, *J* =1.5 Hz), 1.97(s, 3H, Me).
^{13}C NMR (75 MHz, $CDCl_3$): δ =149.46, 141.63, 140.59, 136.13, 130.05, 130.00, 128.31, 127.54, 127.50, 126.47, 125.65, 114.80, 20.08.

***1-(2-ethylphenyl)-1-phenylethene* 3h**[4]

Yield: 0.0289g (9%); colorless liquid.
^{1}H NMR (300 MHz, $CDCl_3$): δ =7.30-7.19(m, 9H, Ar-H), 5.78(d, 1H, vinyl-H, *J* = 1.5 Hz), 5.20(d, 1H, vinyl-H, *J* =1.5 Hz), 2.45-2.38(q, 2H, CH_2), 1.06-1.00(t, 3H, Me).
^{13}C NMR (75 MHz, $CDCl_3$): δ =149.20, 142.16, 141.09, 140.88, 130.21, 128.41, 128.25, 127.69, 127.55, 126.47, 125.55, 114.88, 26.25, 15.16.

***1-(1-Naphthyl)-1-phenylethene* 3i**[3]

Yield: 0.0490g (18%); white crystalline solid, Mp 57-57.9^{o}C.
^{1}H NMR (300 MHz, $CDCl_3$): δ =7.86-7.22(m, 12H, Ar-H), 5.98(d, 1H, vinyl-H, *J* =1.2Hz), 5.38(d, 1H, vinyl-H, *J* =1.2Hz).
^{13}C NMR (75 MHz, $CDCl_3$): δ =148.28, 141.06, 139.80, 133.70, 131.87, 128.36, 128.16, 127.93, 127.68, 127.21, 126.62, 126.42, 125.85, 125.66, 125.40, 116.20.

***1,1-Diphenylethene* 3j**[3]

Yield: 0.0358g (18%); colorless liquid.
^{1}H NMR (300 MHz, $CDCl_3$): δ =7.35-7.30(m, 10H, Ar-H), 5.46(s, 2H, vinyl-H).
^{13}C NMR (75 MHz, $CDCl_3$): δ =150.08, 141.50, 128.26, 128.15, 127.69, 114.24.

***1-(4-Methylphenyl)-1-(pentamethylphenyl)ethene* 5a**[3]

Yield: 0.2206g (78%); white crystalline solid, Mp 85.7-86.3°C.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.20(d, 2H, Ar-H, *J* = 8.4Hz), 7.08(d, 2H, Ar-H, *J* =7.8 Hz), 5.92(d, 1H, vinyl-H, *J* =1.5Hz), 5.00(d, 1H, vinyl-H, *J* =1.5 Hz), 2.32(s, 3H, Me), 2.28(s, 3H, Me), 2.23(s, 6H, 2xMe), 2.09(s, 6H, 2xMe).

^{13}C NMR (75 MHz, $CDCl_3$): δ =148.43, 138.89, 137.22, 137.20, 133.60, 132.28, 131.55, 129.07, 125.91, 113.31, 21.10, 17.83, 16.75, 16.54.

***1-(4-Methylphenyl)-1-(2, 3, 5, 6-tetramethylphenyl)ethene* 5b**[3]

Yield: 0.2198g (84%); white crystalline solid, Mp 115.0-116.8°C.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.18(d, 2H, Ar-H, *J* = 8.4 Hz), 7.09(d, 2H, Ar-H, *J* =8.4 Hz), 6.96(s, 1H, Ar-H), 5.93(d, 1H, vinyl-H, *J* =1.2 Hz), 5.00(d, 1H, vinyl-H, *J* =1.2 Hz), 2.32(s, 3H, Me) , 2.24(s, 6H, 2xMe), 2.03(s, 6H, 2xMe).

^{13}C NMR (75 MHz, $CDCl_3$): δ =147.80, 141.24, 137.30, 136.93, 133.47, 131.96, 130.18, 129.09, 125.84, 113.21, 21.11, 20.13, 16.62.

***1-(3-Bromo-2,4,6-trimethylphenyl)-1-(4-methylphenyl)ethene* 5c**[3]

Yield: 0.2143g (63%); colorless liquid

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.16(d, 2H, Ar-H, *J* = 8.4 Hz), 7.09(d, 2H, Ar-H, *J* =7.8 Hz), 6.99(s, 1H, Ar-H), 5.93(d, 1H, vinyl-H, *J* = 0.9 Hz), 5.00(d, 1H, vinyl-H, *J* =0.9 Hz), 2.42(s, 3H, Me), 2.32(s, 3H, Me), 2.26(s, 3H,Me), 2.06(s, 3H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ =146.87, 140.16, 137.63, 136.70, 136.13(another peak overlapped in this region), 134.89, 129.57, 129.22, 125.71, 125.42, 113.81, 23.93, 21.39, 21.11, 19.88.

***1-(4-Methylphenyl)-1-(2,4,6-trimethylphenyl)ethene* 5d**[3]

Yield: 0.1946g (81%); colorless liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.18(d, 2H, Ar-H, *J* = 8.1 Hz), 7.07(d, 2H, Ar-H, *J* =8.1Hz), 6.90(s, 2H, Ar-H), 5.91(d, 1H, vinyl-H, *J* =1.2 Hz), 5.03(d, 1H, vinyl-H, *J* =1.5 Hz), 2.31(s, 6H, 2xMe), 2.10(s, 6H, 2xMe).

^{13}C NMR (75 MHz, $CDCl_3$): δ =146.68, 138.35, 137.32, 136.71, 136.29, 136.09, 129.11, 128.05, 125.72, 113.50, 21.09, 21.02, 20.03.

***1-(2,5-Dimethylphenyl)-1-(4-methylphenyl)ethene* 5e**[3]

Yield: 0.0214g (9%); colorless liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.17-7.02(m, 7H, Ar-H), 5.71(d, 1H, vinyl-H, *J* = 0.9 Hz), 5.12(d, 1H, vinyl-H, *J* =0.9 Hz), 2.33(s, 6H, 2xMe), 2.01(s, 3H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ =149.32, 141.64, 137.82, 137.30, 134.98, 132.93, 130.61, 129.89, 128.99, 128.07, 126.38, 113.72, 21.11, 20.90, 19.56.

***1-(4-Fluorophenyl)-1-(pentamethylphenyl)ethene* 7a**[3]

Yield: 0.2012g (70%); white crystalline solid, Mp 77.0-77.9^{o}C.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.27[dd, 2H, Ar-H, *J* =7.5(F-H) and 6.9Hz], 6.97[dd, 2H, Ar-H, *J* =8.7(F-H) and 8.7Hz], 5.89(s, 1H, vinyl-H), 5.03(s, 1H, vinyl-H), 2.28(s, 3H, Me), 2.23(s, 6H, 2xMe), 2.09(s, 6H, 2xMe).

^{13}C NMR (75 MHz, $CDCl_3$): δ =162.34(d, $^{1}J_{C\text{-}F}$ =244.8 Hz), 147.58, 138.46, 136.13(d, $^{4}J_{C\text{-}F}$ =3.68 Hz), 133.87, 132.44, 131.44, 127.64(d, $^{3}J_{C\text{-}F}$ =7.43Hz), 115.16(d, $^{2}J_{C\text{-}F}$ =21.0Hz), 113.98, 17.78, 16.76, 16.56.

***1-(4-Fluorophenyl)-1-(2,3,5,6-tetramethylphenyl)ethene* 7b**

Yield: 0.1819g (66%); white crystalline solid, Mp 70.1-72.6^{o}C.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.26-7.21(m, 2H, Ar-H), 6.97-6.92(m, 3H, Ar-H), 5.90(d, 1H, vinyl-H, *J* =1.2 Hz), 5.03(s, 1H, vinyl-H), 2.24(s, 6H, 2xMe), 2.03(s, 6H, 2xMe).

^{13}C NMR (75 MHz, $CDCl_3$): δ =162.37(d, $^{1}J_{C\text{-}F}$ =244.8 Hz), 146.98, 140.82, 135.87(d, $^{4}J_{C\text{-}F}$ =3.08 Hz), 133.64, 131.85, 130.41, 127.57(d, $^{3}J_{C\text{-}F}$ =8.03Hz), 115.19(d, $^{2}J_{C\text{-}F}$ =21.68Hz), 113.87, 20.12, 16.58.

Anal. Calcd. for $C_{18}H_{19}F$: C, 85.00; H: 7.53. found: C, 84.99; H:7.49.

***1-(3-Bromo-2,4,6-trimethylphenyl)-1-(4-fluorophenyl)ethene* 7c**

Yield: 0.1918g (60%); colorless liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.25-7.19(m, 2H, Ar-H), 7.00-6.93(m, 3H, Ar-H), 5.90(d, 1H, vinyl-H, *J* =0.60 Hz), 5.04(s, 1H, vinyl-H), 2.42(s, 3H, Me), 2.26(s, 3H, Me), 2.06(s, 3H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ =162.50(d, $^{1}J_{C\text{-}F}$ =245.4 Hz), 146.00, 139.69, 137.00, 136.04, 135.10(d, $^{4}J_{C\text{-}F}$ =3.68 Hz), 134.80, 129.68, 127.47(d, $^{3}J_{C\text{-}F}$ = 8.03Hz), 125.51, 115.37(d, $^{2}J_{C\text{-}F}$ =21.00Hz), 114.53, 23.94, 21.35, 19.84.

Anal. Calcd. for $C_{17}H_{16}BrF$: C, 63.96; H, 5.05 . found: C, 63.84 ; H: 5.08.

1-(4-Fluorophenyl)-1-(2,4,6-trimethylphenyl)ethene **7d**

Yield: 0.1822g (71%); colorless liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.25-7.21(m, 2H, Ar-H), 6.97-6.91(m, 3H, Ar-H), 5.88(d, 1H, vinyl-H, *J* =0.90 Hz), 5.07(s, 1H, vinyl-H, *J* =1.2 Hz), 2.31(s, 3H, Me), 2.10(s, 6H, 2xMe).

^{13}C NMR (75 MHz, $CDCl_3$): δ =162.44(d, $^1J_{C\text{-}F}$ =247.2 Hz), 145.90, 137.96, 136.57, 135.99, 135.70, 128.22, 127.46(d, $^3J_{C\text{-}F}$ =6.83 Hz), 115.24(d, $^2J_{C\text{-}F}$ = 21.00Hz), 114.19, 21.01, 20.00.

Anal. Calcd. for $C_{17}H_{17}F$: C, 84.96 ; H, 7.13. found: C, 84.94 ; H:7.18.

1-(2,5-Dimethylphenyl)-1-(4-fluorophenyl)ethene **7e**

Yield: 0.1298g (55%); colorless liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.25-7.21(m, 2H, Ar-H), 7.07-6.93(m, 5H, Ar-H), 5.68(d, 1H, vinyl-H, *J* =1.2 Hz), 5.15(s, 1H, vinyl-H, *J* =0.9 Hz), 2.33(s, 3H, Me), 1.99(s, 3H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ =162.38(d, $^1J_{C\text{-}F}$ =245.4 Hz), 148.59, 141.24, 136.83(d, $^4J_{C\text{-}F}$ =2.46 Hz), 135.15, 132.82, 130.57, 130.06, 128.25(d, $^3J_{C\text{-}F}$ =10.5Hz), 128.07, 115.12(d, $^2J_{C\text{-}F}$ =21.68Hz), 114.37, 20.88, 19.53.

Anal. Calcd. for $C_{16}H_{15}F$: C, 84.92 ; H: 6.68. found: C: 84.92; H: 6.77.

(*Z*)*-1-(Pentamethylphenyl)-1,2-diphenylethene* **10a**[3]

Yield: 0.1763g (54%); white crystalline solid, Mp 111.4-115.1°C.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.36-6.91(m, 11H, Ar-H and vinyl-H), 2.31(s, 3H, Me), 2.21(s, 6H, 2xMe), 2.01(s, 6H, 2xMe).

^{13}C NMR (75 MHz, $CDCl_3$): δ =142.20, 141.71, 137.64, 136.27, 133.91, 132.73, 131.16, 128.61, 128.36, 128.14, 127.83, 127.09, 126.72, 126.19, 17.19, 16.87, 16.63.

(*Z*)*-1-(Pentamethylphenyl)-1-phenyl-2-methylethene* **11a**[5]

Yield: 0.1787g (67%); white crystalline solid, Mp 98.0-100.0°C.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.25-7.15(m, 5H, Ar-H), 6.40-6.33(q, 1H, vinyl-H), 2.28(s, 3H, Me), 2.23(s, 6H, 2xMe), 2.04(s, 6H, 2xMe), 1.50-1.48(d, 3H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ =141.80, 141.20, 135.97, 133.32, 132.19, 131.53, 128.22, 126.42, 125.73, 123.24, 17.15, 16.75, 16.62, 15.12.

(*Z*)-*1-(2,3, 5, 6-tetramethylphenyl)-1-phenyl-2-methylethene* 11b

Yield: 0.1625g (62%); white crystalline solid, Mp 77.8-79.0^{o}C.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.25-7.15(m, 5H, Ar-H), 6.95(s, 1H, Ar-H), 6.41-6.34(q, 1H, vinyl-H), 2.24(s, 6H, 2xMe), 1.98(s, 6H, 2xMe), 1.50-1.48(d, 3H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ =141.10, 140.84, 138.53, 133.44, 132.01, 130.16, 128.26, 126.51, 125.68, 123.19, 20.19, 16.04, 15.02.

Anal. Calcd. for $C_{19}H_{22}$: C, 91.14; H: 8.86. found: C, 91.10 ; H :8.82.

(*Z*)-*1-(3-Bromo-2,4,6-trimethylphenyl)-1-phenyl-2-methylethene* 11c[6]

Yield: 0.1682g (49%); colorless viscous liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.27-7.15(m, 5H, Ar-H), 7.01(s, 1H, Ar-H), 6.41-6.34(q, 1H, vinyl-H), 2.42(s, 3H, Me), 2.22(s, 3H, Me), 2.00(s, 3H, Me), 1.53-1.51(d, 3H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ =140.10, 139.92, 137.49, 136.61, 136.23, 135.08, 129.71, 128.38, 126.80, 125.49, 123.83, 23.95, 20.76, 19.51, 14.98.

(*Z*)-*1-(2,4,6-trimethylphenyl)-1-phenyl-2-methylethene* 11d[7]

Yield: 0.1728g (66%); colorless viscous liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.25-7.16(m, 5H, Ar-H), 6.91(s, 2H, Ar-H), 6.40-6.33(q, 1H, vinyl-H), 2.32(s, 3H, Me), 2.04(s, 6H, 2xMe), 1.54-1.51(d, 3H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ =140.46, 139.91, 136.22, 135.58, 128.30, 128.14, 126.57, 125.53(another peak overlapped in this region), 123.28, 21.06, 19.68, 14.97.

(*Z*)-*1-(2,5-Dimethylphenyl)-1-phenyl-2-methylethene* 11e[8]

Yield: 0.1473g (62%); colorless viscous liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.26-6.98(m, 7H, Ar-H), 6.89(s, 1H, Ar-H), 6.31-6.24(q, 1H, vinyl-H), 2.32(s, 3H, Me), 2.04(s, 3H, Me), 1.60-1.58(d, 3H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ=141.57, 141.52, 139.09, 135.02, 133.37, 130.59, 129.88, 128.16, 127.80, 126.55, 126.08, 123.55, 20.95, 18.99, 15.39.

2.4. References

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CHAPTER 3

BF_3 Catalyzed Hydroarylation of Alkynes

A Very Convenient, Simple Procedure for Substituted Arylalkenes from Simple Arenes

3.1. Introduction

Direct functionalization of simple arenes through the formation of new **carbon-carbon** bond has several advantages compared to conventional synthetic methods. In this direct **carbon-carbon** bond formation method aromatic **C-H** bond directly acts as a functional group and participates directly in the reaction. Transition metal-catalyzed hydroarylation reaction of alkynes is one of the attractive methods for the direct formation of **carbon-carbon** bond between arenes and alkynes and provides a direct synthesis of arylalkenes in one step from simple arenes. A well-known method for the direct formation of new **carbon-carbon** bond from aromatic **C-H** bond is the Friedel-Crafts reaction of various arenes, but these reactions require more than equimolar amount of a Lewis acid such as aluminium (**III**) chloride[1].

To date, different methods for the direct functionalization of arenes through the formation of new **carbon-carbon** bond between simple arenes and olefins have been developed, which were catalyzed by transition metals or Lewis acid metals[2]. However, the catalysts used in these developed methods are expensive.

Therefore, it is desirable to seek an efficient, convenient, milder and inexpensive catalyst for the direct functionalization of aromatic compounds.

Literature survey shows that till now the use of $\mathbf{BF_3}$ for the direct formation of **carbon-carbon** bond between arenes and alkynes through the hydroarylation reaction has not attracted the attention of the chemists.

In this chapter, a more convenient and very simple direct **carbon-carbon** bond formation method between electron rich arenes and arylsubstituted alkynes using very simple inexpensive Lewis acid, $\mathbf{BF_3}$ is reported.

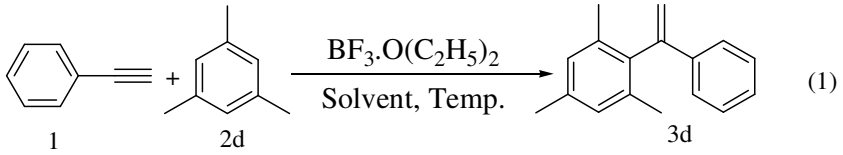
3.2. Results and Discussion

3.2.1. *Optimization of the reaction conditions*

Direct preparation of 1,1-diarylalkenes was carried out from the corresponding arenes and alkynes using the Lewis acid $\mathbf{BF_3}$ as a catalyst in the presence of

dichloroethane solvent at 50°C. In the present study, to optimize the reaction conditions initially, the work was confined on the efficiency of the hydroarylation reaction of phenylacetylene **1** with mesitylene **2d** in the presence of $\mathbf{BF_3}$ catalyst (**Scheme 1**). The results are given in **Table 1**.

Scheme 1. Hydroarylation reaction of phenylacetylene **1** with mesitylene **2d** in the presence of $\mathbf{BF_3}$ catalyst under different reaction conditions.



(1)

Table 1. Hydroarylation reaction of phenylacetylene **1** with mesitylene **2d** in the presence of $\mathbf{BF_3}$ catalyst under different reaction conditions**.**

Entry	Arene **2d** (mmol)	Temp.°C	Product **3d**	Yield(%)[a]
1	2d	30	3d	53[b]
2	2d	30	3d	55[c]
3	2d	30	3d	17[d]
4	2d	30	3d	52[e]
5	**2d**	**50**	**3d**	**57[f]**
6	2d	60	3d	54[g]
7	2d	50	No Product	-[h]
8	2d	50	3d	56[f,i]

***Reaction conditions*:** Mesitylene **2d** (5.0 mmol), phenylacetylene **1**(1.0 mmol), $\mathbf{BF_3.(OC_2H_5)_2}$ (1.0 mmol), CH_2Cl_2(2.0 mL) at 30°C for 24 hours.

[a]Isolated yield based on phenylacetylene **1**.

[b]Molecular sieve **4A**(0.2131g) was used.

[c]CH_2Cl_2 (0.5mL) was used and no molecular sieve was used.

[d]$BF_3.(OC_2H_5)_2$ (2.0 mmol) and molecular sieve **4A**(0.2128g) were used.

[e]$BF_3.(OC_2H_5)_2$ (2.0 mmol), CH_2Cl_2(0.5 mL) were used and no molecular sieve was used.

[f]$(CH_2)_2Cl_2$ (0.5mL) at 50°C.

[g]$(CH_2)_2Cl_2$ (0.5mL) at 60°C.

[h]3-butyn-2-one (1.0 mmol), $(CH_2)_2Cl_2$ (0.5mL) at 50°C.

[i]H_2O(1.0 mmol) was used.

The reaction using **BF_3** catalyst at 30°C for 24 hours in the presence of CH_2Cl_2 (2.0 mL) and molecular sieve afforded the hydroarylation product **3d** in 53% yield (Entry 1). When the reaction was carried out using less amount of CH_2Cl_2 (0.5 mL) in the absence of molecular sieve improved the yield of the hydroarylation product **3d** (Entry 2). Increasing the amount of **BF_3** did not improve the yield (Entries 3, 4). When the reaction was carried out at 50°C then improved the yield but at 60°C decreased the yield (Entries 5 and 6). No hydroarylation reaction occurred when the reaction was carried out with the alkyne, 3-butyn-2-one (Entry 7). When the reaction was carried out using equimolar amount of **BF_3** and water then afforded 56% of the hydroarylation product **3d** (Entry 8). From the above screening results it was found that the entry 5 is the optimum condition for the reaction.

3.2.2. Scope of the hydroarylation reaction

Using the reaction conditions of Entry 5 the hydroarylation reaction of phenylacetylene **1** was further conducted with different electron rich arenes **2** **(Scheme 2)**. The results are given in **Table 2.**

Scheme 2. Hydroarylation reaction of phenylacetylene **1** with different electron rich arenes **2** in the presence of **$BF_3.O(C_2H_5)_2$** catalyst.

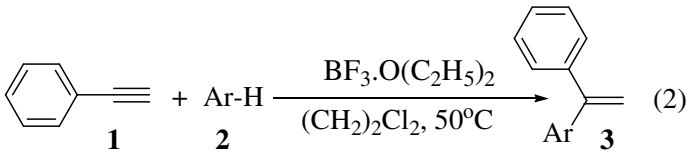
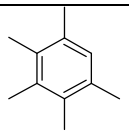
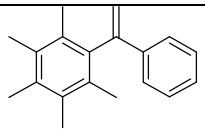
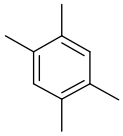
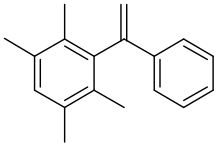
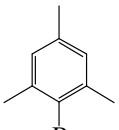
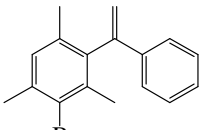
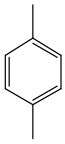
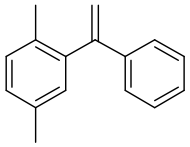


Table 2. Hydroarylation reaction of phenylacetylene **1** with different electron rich arenes **2** in the presence of **$BF_3.O(C_2H_5)_2$** catalyst[a].

Entry	Arene 2	Time(h)	Product 3	Yield (%)[b]
1	 2a	24	 3a	55
2	 2b	24	 3b	51

3	 2c		36	 3c	32
4	 2e		24	 3e	39

[a]***Reaction conditions*:** Arene **2**(5.0 mmol), phenylacetylene **1** (1.0 mmol), **$BF_3.O(C_2H_5)_2$** (1.0 mmol), $(CH_2)_2Cl_2$ (0.5mL) at 50°C.

[b]Isolated yield based on phenylacetylene **1**.

The hydroarylation reaction of electron rich arenes **2** such as pentamethylbenzene **2a**, 1,2,4,5-tetramethylbenzene **2b**, 1-bromo-2,4,6-trimethylbenzene **2c**, and 1,4-dimethylbenzene **2e** with phenylacetylene **1** afforded 1-aryl-1-phenylethenes **3** in moderate yields (Entries 1-4).

Next, the hydroarylation reactions of 4-methylphenylacetylene **4**, with different electron rich arenes **2** was carried out under the same reaction conditions (**Scheme 3**) as that of the reaction of phenylacetylene **1** with different arenes **2**. The results are given in **Table 3.** In the reaction of 4-methylphenylacetylene **4** with electron rich arenes **2a, 2b** and **2d** excellent yields of the hydroarylation products **5** were obtained (Entries 1, 2 and 4). However, the reaction with 1-bromo-2,4,6-trimethylbenzene **2c** and *p*-xylene **2e** resulted in a low yield of the hydroarylation products **5c** and **5e** (Entries 3 and 5) respectively.

Scheme 3. Hydroarylation reaction of 4-methylphenylacetylene **4** with different electron rich arenes **2** in the presence of **$BF_3.O(C_2H_5)_2$** catalyst.

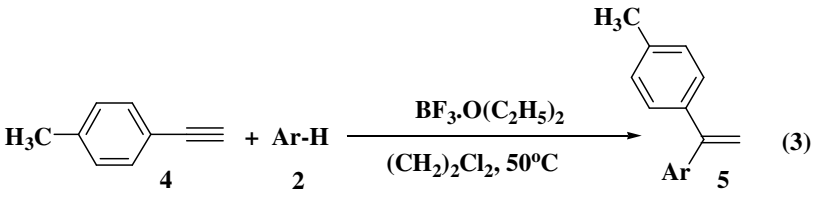
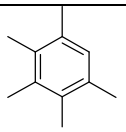
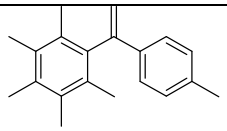
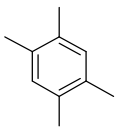
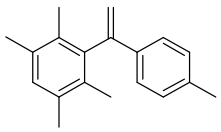
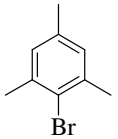
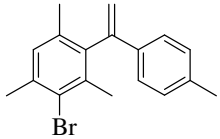
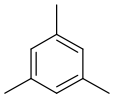
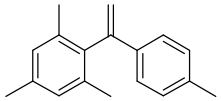
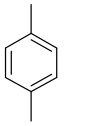
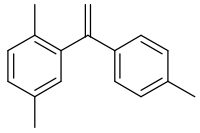


Table 3. Hydroarylation reaction of 4-methylphenylacetylene **4** with different electron rich arenes **2** in the presence of $\mathbf{BF_3.O(C_2H_5)_2}$ catalyst[a].

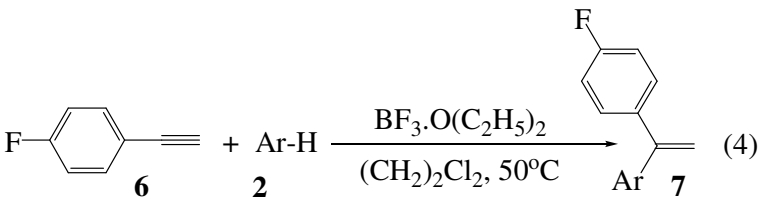
Entry	Arene 2	Time(h)	Product **5**	Yield (%)[b]
1	 2a	24	 5a	65
2	 2b	24	 5b	65
3	 Br 2c	36	 Br 5c	44
4	 2d	24	 5d	73
5	 2e	24	 5e	40

[a]***Reaction conditions***: Arene **2** (5.0 mmol), 4-methylphenylacetylene **4** (1.0 mmol), $\mathbf{BF_3.O(C_2H_5)_2}$ (1.0 mmol), $(CH_2)_2Cl_2$ (0.5mL) at 50°C.

[b]Isolated yield based on 4-methylphenylacetylene **4.**

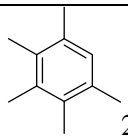
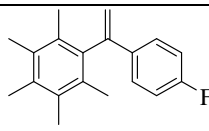
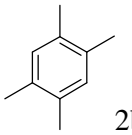
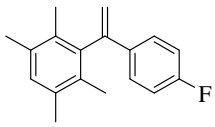
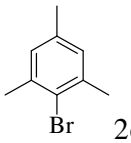
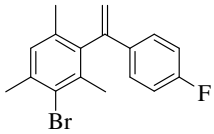
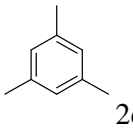
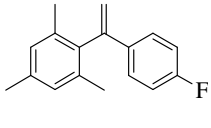
Again, the reaction of an electron withdrawing group containing alkyne, 4-fluorophenylacetylene **6** was examined with various electron rich arenes **2** under the above reaction conditions (**Scheme 4**). The results of the reactions are shown in **Table 4**. The reaction of electron rich arenes **2a-2d** gave the hydroarylation products **7** in moderate to low yields (Entries 1-5).

Scheme 4. Hydroarylation reaction of 4-fluorophenylacetylene **6** with different electron rich arenes **2** in the presence of $\mathbf{BF_3.O(C_2H_5)_2}$ catalyst.



6 **2** **7**

Table 4. Hydroarylation reaction of 4-fluorophenylacetylene **6** with different electron rich arenes **2** in the presence of $\mathbf{BF_3.O(C_2H_5)_2}$ catalyst[a].

Entry	Arene **2**	Time(h)	Product **7**	Yield (%)[b]
1	 2a	24	 7a	44
2	 2b	24	 7b	50
3	 2c	36	 7c	41
4	 2d	24	 7d	43

[a]***Reaction conditions***: Arene **2** (5.0 mmol), 4-fluorophenylacetylene **6** (1.0 mmol), $\mathbf{BF_3.O(C_2H_5)_2}$ (1.0 mmol), $(CH_2)_2Cl_2$ (0.5mL) at 50°C.

[b]Isolated yield based on 4-fluorophenylacetylene **6.**

Finally, the hydroarylation reaction of internal alkyne 1-methyl-2-phenylacetylene **8** was examined with various electron rich arenes **2** under the above reaction conditions (**Scheme 5**). The results of the reactions are shown in **Table 5**. The reaction of 1-methyl-2-phenylacetylene **8** with pentamethylbenzene **2a,** 1,2,4,5-tetramethylbenzene **2b**, 1-bromo-2,4,6-trimethylbenzene **2c**, and 1,4-dimethylbenzene **2e** afforded 1-aryl-1-phenylethenes **9** in moderate yields (Entries 1-3 and 5). An excellent yield of the hydroarylation product **9d** was obtained when the reaction was carried out with the electron rich arenes 1,3,5-trimethylbenzene **2d (**Entry 4**).**

Scheme 5. Hydroarylation reaction of internal alkyne **8** with different electron rich arenes **2** in the presence of $\mathbf{BF_3.O(C_2H_5)_2}$ catalyst.

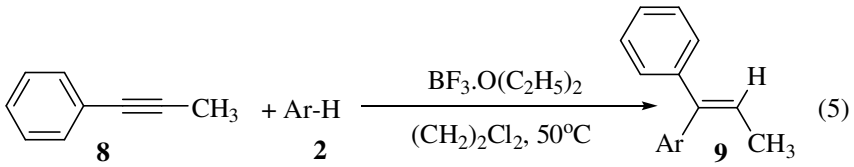
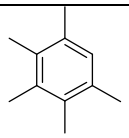
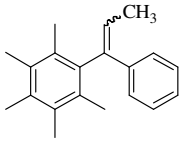
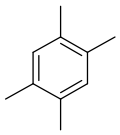
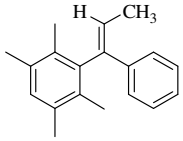
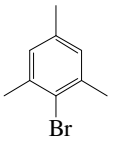
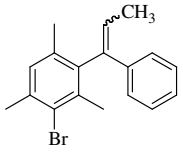
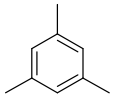
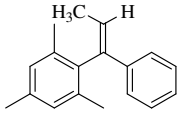
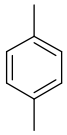
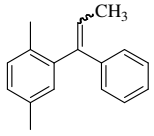


Table 5. Hydroarylation reaction of internal alkyne **8** with different electron rich arenes **2** in the presence of **$BF_3.O(C_2H_5)_2$** catalyst[a].

Entry	Arene 2	Time(h)	Product **9**	Yield (%)[b]
1	 2a	30	 9a	35[c]
2	 2b	30	 9b	31
3	 2c	36	 9c	25[c]
4	 2d	30	 9d	70
5	 2e	30	 9e	56[c]

[a]***Reaction conditions***: Arene **2** (5.0 mmol), 1-methyl-2-phenylacetylene **8** (1.0 mmol), **$BF_3.O(C_2H_5)_2$** (1.0 mmol), $(CH_2)_2Cl_2$ (0.5mL) at 50°C.

[b]Isolated yield based on 1-methyl-2-phenylacetylene **8.**

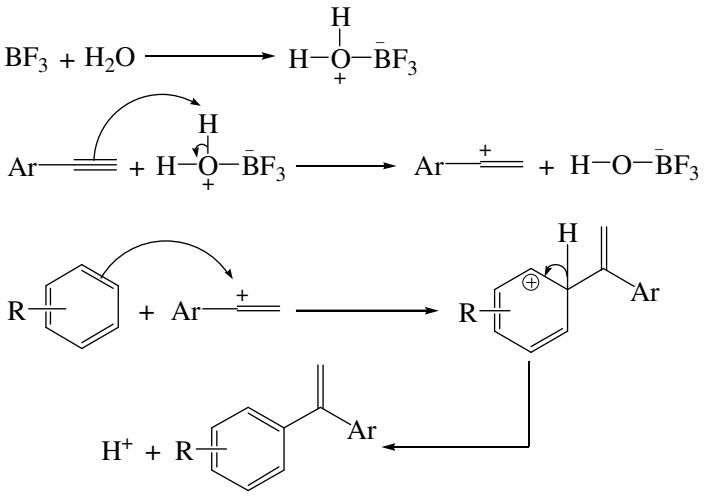
[c]Mixture of *E*- and *Z*-isomer was formed.

3.2.3. *Possible mechanism of the $BF_3.O(C_2H_5)_2$ catalyzed hydroarylation reaction*

The hydroarylation reaction between arenes and arylsubstituted alkynes in the presence of **$BF_3.O(C_2H_5)_2$** is considered to be a Friedel-Crafts type reaction (**Scheme 6**). It has been observed that in **BF_3** catalyzed hydroarylation reaction **BF_3** directly does not act as a catalyst. First of all **BF_3** rapidly reacts with

atmospheric moisture / water and forms a hydrogen ion source $\mathbf{H_2O^+\text{-}BF_3^-}$**.** An alkyne reacts with a hydrogen ion of the resulting hydrogen ion source, $\mathbf{H_2O^+\text{-}BF_3^-}$ and forms arylvinyl cation. The resulting arylvinyl cation then undergoes electrophilic aromatic substitution reaction with an electron rich arene to give the desire hydroarylation product, 1,1-diarylalkene.

Scheme 6. Mechanism of the $BF_3.O(C_2H_5)_2$ catalyzed hydroarylation of alkynes



In summary, the author has demonstrated that the $\mathbf{BF_3.O(C_2H_5)_2}$ catalyzed hydroarylation reaction of alkynes proceeds smoothly and efficiently when arylsubstituted alkynes and electron rich arenes are used. The simplicity of this procedure along with the mildness is practical as a synthetic tool of arylalkenes.

3.3. Experimental Section

General

All solvents and starting materials were used during the research works as received without further purification unless otherwise indicated. ^{1}H NMR and ^{13}C NMR were recorded on a JEOL JNM-Al-300FT-NMR spectrometer in $CDCl_3$ solution (TMS as an internal standard). Melting points of the pure compounds were recorded by thin disc method on a YANACO electrothermal melting point apparatus and are uncorrected.

General procedure for the hydroarylation of alkynes

Required molar amount of $\mathbf{BF_3.O(C_2H_5)_2}$(1.0 mmol), $(CH_2)_2Cl_2$ (0.5 mL), arene (5.0 mmol) and alkyne (1.0 mmol) were taken in a 25.0 mL quick-fit round bottom flask and stirred at 50°C temperature until the completion of the reaction. After the completion of the reaction the reaction mixture was poured into 20.0 mL of water. The aqueous reaction mixture was then extracted with dichloromethane (4 x 10.0 mL) and dried over anhydrous sodium sulfate. Finally, dichloromethane was removed under reduced pressure below 40°C**.** Individual pure compounds were isolated from the reaction mixture by column chromatography using silica gel as a stationary phase.

1-(Pentamethylphenyl)-1-phenylethene 3a[3]

Yield: 0.1407g (55 %); white crystalline solid, Mp 70.0-71.6°C.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.31-7.24(m, 5H, Ar-H), 5.97(d, 1H, vinyl-H, *J* =1.5Hz), 5.07(d, 1H, vinyl-H, *J* =1.5Hz), 2.29(s, 3H, Me), 2.24(s, 6H, 2xMe), 2.10(s, 6H, 2xMe).

^{13}C NMR (75 MHz, $CDCl_3$): δ =148.58, 139.98, 138.67, 133.72, 132.33, 131.56, 128.35, 127.41, 125.99, 114.31, 17.86, 16.79, 16.57.

***1-Phenyl-(2,3,5,6-tetramethylphenyl)ethene 3b*[3]**

Yield: 0. 1338g (51%); white crystalline solid, Mp 66.9-68.0°C.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.29-7.23(m, 5H, Ar-H), 6.97(s, 1H, Ar-H), 5.98(d, 1H, vinyl-H, *J* =1.5Hz), 5.07(d, 1H, vinyl-H, *J* =1.5Hz), 2.25(s, 6H, 2xMe), 2.04(s, 6H, 2xMe).

^{13}C NMR (75 MHz, $CDCl_3$): δ =147.99, 141.04, 139.72, 133.51, 131.96, 130.27, 128.36, 127.47, 125.91, 114.18, 20.16, 16.66.

***1-(3-Bromo-2,4,6-trimethylphenyl)-1-phenylethene 3c*[3]**

Yield: 0.0968g (32%); colorless liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.32-7.24(m, 5H, Ar-H), 7.00(s, 1H, Ar-H), 5.98(d, 1H, vinyl-H, *J* =1.2Hz), 5.07(d, 1H, vinyl-H, *J* =1.2Hz), 2.42(s, 3H, Me), 2.27(s, 3H, Me), 2.07(s, 3H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ =147.01, 139.93, 138.92, 136.81, 136.12, 134.90, 129.59, 128.49, 127.77, 125.78, 125.44, 114.81, 23.97, 21.42, 19.93.

***1-Phenyl-1-(2,4,6-trimethylphenyl)ethene 3d*[3]**

Yield: 0.1305g (57%); colorless liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.28-7.24(m, 5H, Ar-H), 6.91(s, 2H, Ar-H), 5.95(d, 1H, vinyl-H, *J* =1.5Hz), 5.09 (d, 1H, vinyl-H, *J* =1.5Hz), 2.32(s, 3H, Me), 2.11(s, 6H, 2xMe).

^{13}C NMR (75 MHz, $CDCl_3$): δ =146.83, 139.51, 138.14, 136.39, 136.08, 128.38, 128.08, 127.51, 125.79, 114.48, 21.02, 20.07.

***1-(2,5-Dimethylphenyl)-1-phenylethene 3e*[3]**

Yield: 0.0853g (39%); colorless liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.29-7.24(m, 5H, Ar-H), 7.06(m, 2H, Ar-H), 7.04(m, 1H, Ar-H), 5.75(d, 1H, vinyl-H, *J* =1.5Hz), 5.18(d, 1H, vinyl-H, *J* =1.5Hz), 2.34(s, 3H, Me), 2.01(s, 3H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ =149.54, 141.43, 140.63, 135.01, 132.91, 130.65, 129.94, 128.28, 128.16, 127.48, 126.47, 114.62, 20.89, 19.59.

***1-(4-Methylphenyl)-1-(pentamethylphenyl)ethene 5a*[3]**

Yield: 0.1809g (65%); white crystalline solid, Mp 84.6-85.8^{o}C.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.20(d, 2H, Ar-H, *J* = 8.1Hz), 7.09(d, 2H, Ar-H, *J* = 8.1 Hz), 5.93(d, 1H, vinyl-H, *J* =1.5 Hz), 5.00(d , 1H, vinyl-H, *J* =1.2 Hz), 2.32(s, 3H, Me), 2.29(s, 3H, Me), 2.23 (s, 6H, 2xMe), 2.09(s, 6H, 2xMe).

^{13}C NMR (75 MHz, $CDCl_3$): δ =148.41, 138.87, 137.21, 137.18, 133.59, 132.28, 131.55, 129.07, 125.90, 113.31, 21.10, 17.83, 16.75, 16.54.

***1-(4-Methylphenyl)-1-(2,3,5,6-tetramethylphenyl)ethene 5b*[3]**

Yield: 0.1688g (65%); white crystalline solid, Mp 113.8-115.3^{o}C.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.18(d, 2H, Ar-H, *J* = 8.1 Hz), 7.09(d, 2H, Ar-H, *J* = 8.1 Hz), 6.96(s, 1H, Ar-H), 5.93(d, 1H, vinyl-H, *J* =1.2 Hz), 5.00(d, 1H, vinyl-H, *J* =1.2 Hz), 2.32(s, 3H, Me) , 2.24(s, 6H, 2xMe), 2.04(s, 6H, 2xMe).

^{13}C NMR (75 MHz, $CDCl_3$): δ =147.82, 141.24, 137.28, 136.94, 133.46, 131.95, 130.19, 129.09, 125.84, 113.20, 21.10, 20.13, 16.62.

***1-(3-Bromo-2,4,6-trimethylphenyl)-1-(4-methylphenyl)ethene 5c*[3]**

Yield: 0.1453g (44%); colorless liquid

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.16(d, 2H, Ar-H, *J* =8.4 Hz), 7.10(d, 2H, Ar-H, *J* =8.4 Hz), 6.99(s, 1H, Ar-H), 5.93(d, 1H, vinyl-H, *J* =1.2 Hz), 5.01(d, 1H, vinyl-H, *J* =1.2 Hz), 2.42(s, 3H, Me), 2.33(s, 3H, Me), 2.26(s, 3H,Me), 2.06(s, 3H, Me).
^{13}C NMR (75 MHz, $CDCl_3$): δ =146.79, 140.11, 137.62, 136.68, 136.09, 136.07, 134.87, 129.55, 129.20, 125.68, 125.40, 113.81, 23.95, 21.39, 21.11, 19.89.

***1-(4-Methylphenyl)-1-(2,4,6-trimethylphenyl)ethene 5d*[3]**

Yield: 0.1824g (73%); colorless liquid.
^{1}H NMR (300 MHz, $CDCl_3$): δ =7.18(d, 2H, Ar-H, *J* = 8.1 Hz), 7.08(d, 2H, Ar-H, *J* = 8.1Hz), 6.90(s, 2H, Ar-H), 5.91(d, 1H, vinyl-H, *J* =1.2 Hz), 5.03(d, 1H, vinyl-H, *J* =1.2 Hz), 2.32(s, 6H, 2xMe), 2.11(s, 6H, 2xMe).
^{13}C NMR (75 MHz, $CDCl_3$): δ =146.64, 138.33, 137.29, 136.67, 136.27, 136.07, 129.10, 128.05, 125.69, 113.48, 21.08, 21.02, 20.03.

***1-(2,5-Dimethylphenyl)-1-(4-methylphenyl)ethene 5e*[3]**

Yield: 0.1025g (40%); colorless liquid.
^{1}H NMR (300 MHz, $CDCl_3$): δ =7.18-7.03(m, 7H, Ar-H), 5.71(d, 1H, vinyl-H, *J* = 1.5 Hz), 5.12(d, 1H, vinyl-H, *J* =1.5 Hz), 2.33 (s, 6H, 2xMe), 2.01(s, 3H, Me).
^{13}C NMR (75 MHz, $CDCl_3$): δ =149.30, 141.62, 137.79, 137.27, 134.96, 132.91, 130.60, 129.90, 128.99, 128.07, 126.36, 113.73, 21.11, 20.90, 19.58.

***1-(4-Fluorophenyl)-1-(pentamethylphenyl)ethene 7a*[3]**

Yield: 0.1403g (44%); white crystalline solid, Mp 75.9-76.0^{o}C.
^{1}H NMR (300 MHz, $CDCl_3$): δ =7.28[dd, 2H, Ar-H, *J* =7.8 (F-H) and 6.6Hz], 6.98[dd, 2H, Ar-H, *J* =8.7(F-H) and 9.0Hz], 5.90(d, 1H, vinyl-H, *J* =1.2Hz), 5.04(d, 1H, vinyl-H, *J* =1.2 Hz), 2.29(s, 3H, Me), 2.24(s, 6H, 2xMe), 2.09(s, 6H, 2xMe).
^{13}C NMR (75 MHz, $CDCl_3$): δ =162.33(d, $^1J_{C\text{-}F}$ =245.4 Hz), 147.57, 138.45, 136.12(d, $^4J_{C\text{-}F}$ =3.08 Hz), 133.87, 132.44, 131.44, 127.64(d, $^3J_{C\text{-}F}$ =7.43Hz), 115.16(d, $^2J_{C\text{-}F}$ =21.0Hz), 113.98, 17.78, 16.76, 16.56.

1-(4-Fluorophenyl)-1-(2,3,5,6-tetramethylphenyl)ethene 7b

Yield: 0.1364g (50%); white crystalline solid, Mp 69.0-70.6^{o}C.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.26-7.21(m, 2H, Ar-H), 6.98-6.92(m, 3H, Ar-H), 5.91(d, 1H, vinyl-H, *J* =0.9 Hz), 5.04(s, 1H, vinyl-H), 2.25(s, 6H, 2xMe), 2.03(s, 6H, 2xMe).

^{13}C NMR (75 MHz, $CDCl_3$): δ =162.33(d, $^{1}J_{C\text{-}F}$ =244.73 Hz), 146.90, 140.77, 135.82(d, $^{4}J_{C\text{-}F}$ =3.08 Hz), 133.64, 131.86, 130.37, 127.55(d, $^{3}J_{C\text{-}F}$ =7.43Hz), 115.18(d, $^{2}J_{C\text{-}F}$ =21.08Hz), 113.90, 20.16, 16.60.

1-(3-Bromo-2,4,6-trimethylphenyl)-1-(4-fluorophenyl)ethene 7c

Yield: 0.1357g (41%); colorless liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.26-7.20(m, 2H, Ar-H), 7.00-6.93(m, 3H, Ar-H), 5.91(s, 1H, vinyl-H), 5.04(s, 1H, vinyl-H), 2.42(s, 3H, Me), 2.26(s, 3H, Me), 2.06(s, 3H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ =162.47(d, $^{1}J_{C\text{-}F}$ =245.4 Hz), 145.93, 139.65, 136.98, 136.03, 135.05(d, $^{4}J_{C\text{-}F}$ =3.75 Hz), 134.80, 129.67, 127.45(d, $^{3}J_{C\text{-}F}$ = 8.03Hz), 125.49, 115.36(d, $^{2}J_{C\text{-}F}$ =21.68Hz), 114.54(d, *J* =1.88 Hz), 23.97, 21.36, 19.87.

1-(4-Fluorophenyl)-1-(2,4,6-trimethylphenyl)ethene 7d

Yield: 0.1091g (43%); colorless liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.26-7.21(m, 2H, Ar-H), 6.98-6.92(m, 4H, Ar-H), 5.88(s, 1H, vinyl-H), 5.07(s, 1H, vinyl-H), 2.32(s, 3H, Me), 2.10(s, 6H, 2xMe).

^{13}C NMR (75 MHz, $CDCl_3$): δ =162.38(d, $^{1}J_{C\text{-}F}$ =244.8Hz), 145.75, 137.87, 136.57, 136.00, 135.61(d, $^{4}J_{C\text{-}F}$ =3.08 Hz), 128.16, 127.42(d, $^{3}J_{C\text{-}F}$ =8.03 Hz), 115.22(d, $^{2}J_{C\text{-}F}$ =21.08Hz), 114.21(d, $J_{C\text{-}F}$ =1.88 Hz), 21.02, 20.01.

***1-(Pentamethylphenyl)-1-phenyl-2-methylethene 9a*[4]**

Yield: 0.0989g (35%); colorless viscous liquid. Mixture of *E*- and *Z*-isomers (50:50).

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.30-7.13(m, 10H, Ar-H), 6.40-6.33(q, 1H, vinyl-H), 5.63-5.56(q, 1H, vinyl-H), 2.28(s, 3H, Me), 2.25 (s, 3H, Me), 2.23(s, 6H, 2xMe), 2.21(s, 6H, 2xMe), 2.16(s, 6H, 2xMe), 2.04(s, 6H, 2xMe), 2.01-1.98(d, 3H, Me), 1.50-1.48(d, 3H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ =141.80, 1.41.61, 141.32, 141.19, 139.88, 135.97, 133.38, 133.32, 132.27, 132.19, 131.81, 131.52, 129.17, 128. 22, 127.79, 126.42, 126.24, 125.91, 125.73, 123.22, 18.09, 17.14, 16.75, 16.61, 15.46, 15.12.

(E)-1-(2,3,5,6-tetramethylphenyl)-1-phenyl-2-methylethene 9b

Yield: 0.0816g (31%); white crystalline solid, Mp 84.5-85.8^{o}C.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.31-7.16(m, 5H, Ar-H), 6.91(s, 1H, Ar-H), 5.63-5.56(q, 1H, vinyl-H), 2.22(s, 6H, 2xMe), 2.10(s, 6H, 2xMe), 2.02-1.99(d, 3H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ =143.79, 140.57, 139.56, 133.46, 132.22, 130.00, 129.15, 127.78, 126.29, 125.89, 20.27, 16.92, 15.44.

1-(3-Bromo-2,4,6-trimethylphenyl)-1-phenyl-2-methylethene 9c [5]

Yield: 0.0898g (25%); colorless viscous liquid. Mixture of *Z*- and *E*-isomers (86:14).

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.38-7.14(m, 10H, Ar-H), 7.01 (s, 1H, Ar-H), 6.94(s, 1H, Ar-H), 6.42-6.35(q, 1H, vinyl-H), 5.65-5.57(q, 1H, vinyl-H), 2.42(s, 3H, Me), 2.38(s, 6H, 2xMe), 2.33(s, 6H, 2xMe), 2.22(s, 3H, Me), 2.10(s, 6H, 2xMe), 2.05(s, 3H, Me), 2.02-1.99(d, 3H, Me), 1.53-1.51(d, 3H, Me).

(Z)-1-(2,4,6-trimethylphenyl)-1-phenyl-2-methylethene 9d [2e]

Yield: 0.1698g (70%); colorless viscous liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.26-7.17(m, 5H, Ar-H), 6.92(s, 2H, Ar-H), 6.40-6.33(q, 1H, vinyl-H), 2.32(s, 3H, Me), 2.04(s, 6H, 2xMe), 1.54-1.52(d, 3H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ =140.42, 139.82, 136.21, 136.18, 135.55, 128.28, 128.11, 126.56, 125.49, 123.30, 21.07, 19.69, 14.98.

1-(2,5-Dimethylphenyl)-1-phenyl-2-methylethene 9e [6]

Yield: 0.1497g (56%); colorless viscous liquid. Mixture of *E*-and *Z*-isomers (82:18).

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.32-6.89(m, 16H, Ar-H), 6.31-6.24(q, 1H, vinyl-H), 5.80-5.73(q, 1H, vinyl-H), 2.32(s, 3H, Me), 2.05(s, 3H, Me), 2.03(s, 3H, Me), 1.97(s, 3H, Me), 1.91-1.89(d, 3H, Me), 1.61-1.58(d, 3H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ =143.88, 142.49, 141.53, 141.49, 140.05, 139.07, 135.01, 134.76, 133.35, 132.92, 130.88, 130.57,130.02, 129.86, 129.41, 128.16,

127.81, 127,79, 127.62, 126.54, 126.42, 126.05, 125.82, 123.55, 20.95, 20.87, 19.89, 18.99, 15.40, 15.35.

3.4. References

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CHAPTER 4

Metal-free Hydroarylation of Alkynes

A Very Convenient, Simple Procedure for Substituted Arylalkenes

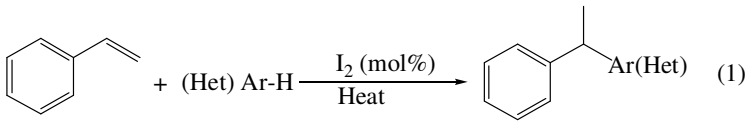
4.1. Introduction

Catalytically direct activation of unreactive aromatic **C-H** bond followed by functionalization such as **carbon-carbon** bond formation has several advantages compared to conventional synthetic methods. This direct **carbon-carbon** bond formation method does not require the pre-functionalization like halogenation of aromatic **C-H** bond, because in this direct **carbon-carbon** bond formation method aromatic **C-H** bond directly acts as a functional group and participates directly in the reaction instead of reactive groups as the reaction site for the functionalization. This direct **carbon-carbon** bond formation method not only reduces the reaction steps but also avoids the use of toxic halogenated compounds. Transition metal-catalyzed hydroarylation reaction of alkynes is one of the attractive methods for the direct formation of **carbon-carbon** bond between arenes and alkynes and provides a direct synthesis of arylalkenes in one step from simple arenes. Historically, Friedel-Crafts reactions of aromatic compounds have been employed for the direct formation of **carbon-carbon** bond, but these reactions require more than equimolar amount of a Lewis acid such as aluminium (**III**) chloride[1]. Recently, direct hydroarylation reaction of alkenes or alkynes using transition metals or Lewis acid metals has attracted considerable attention in organic synthesis[2].

No doubt the metal-catalyzed hydroarylation reactions so far discussed are excellent, efficient and powerful methods for the direct formation of new **carbon-carbon** bond between arenes and alkynes. But still there are some limitations, such as to carry out a transition metal-catalyzed hydroarylation reaction requires high temperature, strong acidic conditions and special cautions for handling metal catalysts under inert atmosphere. Furthermore, contamination of pharmaceutical materials with a trace amount of metals in the processes of manufacture causes a serious problem. These drawbacks of the transition metal-catalyzed hydroarylation reactions have attracted the attention to develop a more convenient, simple and efficient synthetic method for the hydroarylation of alkynes without the involvement of transition metals. A very recent paper reported an efficient oxidative cleavage of double bonds as a synthetic application of arylated alkenes[3] which encouraged studying the hydroarylation reaction of alkynes.

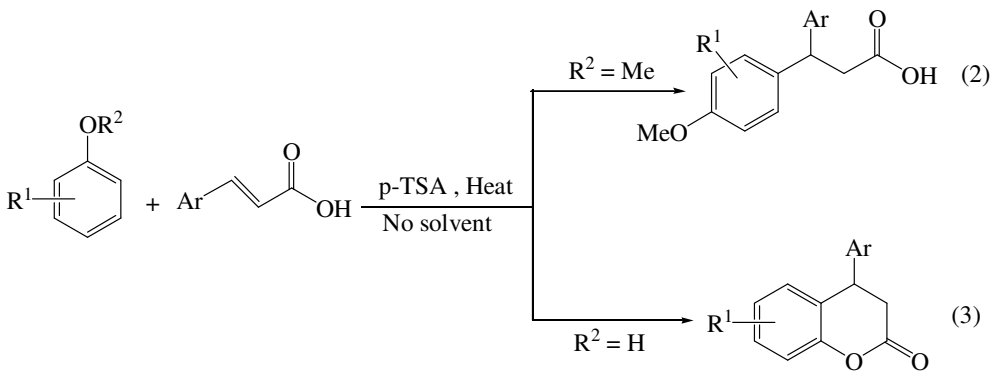
Very recently, Yao *et al* reported that molecular iodine mediates the hydroarylation reaction of styrenes with arenes and heteroarenes in the absence of any solvent and transition metals to afford 1,1-diarylalkanes in good to high yields (**Scheme 1**)[4].

Scheme 1



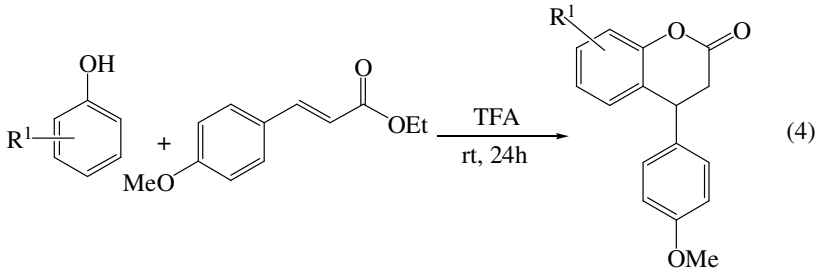
Hydroarylation of cinnamic acids with anisoles and phenols in the presence of *p*-toluenesulfonic acid (*p*-TSA) under metal and solvent-free conditions afforded 3-(4-methoxyphenyl)-3-phenylpropionic acids and dihydrocoumarins, respectively, in high yields and excellent selectivity (**Scheme 2**)[5].

Scheme 2



Kitamura *et al* reported that cinnamic acid derivatives undergo intermolecular hydroarylation reaction with phenols in the presence of trifluoroacetic acid without the involvement of transition metals and give dihydrocoumarins in good to high yields (**Scheme 3**)[6].

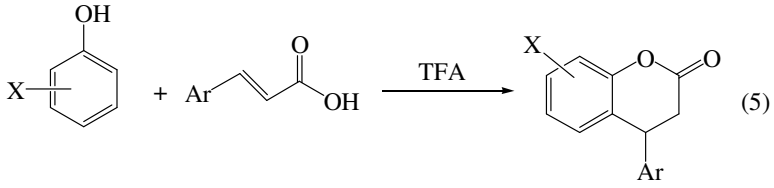
Scheme 3



(4)

On the other hand, Tunge *et al* further reported that cinnamic acids undergo intermolecular hydroarylation reaction with phenols in the presence of trifluoroacetic acid without the involvement of transition metals and afford dihydrocoumarins and dihydroquinolones in good yields (**Scheme 4**)[7].

Scheme 4



(5)

To date, although a number of papers have been reported about the hydroarylation reaction of alkenes with arenes, which were carried out under metal-free conditions. Literature survey reveals that still there is no report on the hydroarylation reaction of alkynes with arenes under metal-free conditions.

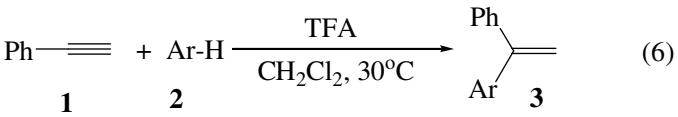
4.2. Results and Discussion

Direct preparation of 1,1-diarylalkenes was carried out from the corresponding arenes and alkynes using trifluoroacetic acid in CH_2Cl_2 solvent at 30^oC without using any transition metals and additives. In the present study, to optimize the hydroarylation reaction initially, the work was concentrated on the efficiency of the hydroarylation reaction of phenylacetylene **1** with arenes **2** in the presence of trifluoroacetic acid (TFA) in CH_2Cl_2 solvent at 30^oC (**Scheme 5**). The results of this hydroarylation reaction are given in **Table 1**.

First of all, the reaction of phenylacetylene **1** (1.0 mmol) with pentamethylbenzene **2a** (1.0 mmol) in the presence of TFA (1.0 mL) in CH_2Cl_2 solvent at 30°C for 18 hours afforded hydroarylation product, 1-aryl-1-phenylethene **3a** in 42% yield (Entry 1). When the reaction of phenylacetylene **1** (1.0 mmol) was carried out with increasing amount of pentamethylbenzene **2a** (10.0 mmol) in the presence of TFA (1.0 mL) in CH_2Cl_2 solvent at 30°C for 48 hours afforded hydroarylation product, 1-aryl-1-phenylethene **3a** in 93 % yield (Entry 2)**.**

Again, the reaction of phenylacetylene **1** (1.0 mmol) and pentamethylbenzene **2a** (10.0 mmol) in the presence of reduce amount of TFA (0.15 mL) in CH_2Cl_2 solvent at 30°C for 48 hours afforded hydroarylation product, 1-aryl-1-phenylethene **3a** in 65 % yield (Entry 3)**.** Using the reaction conditions of Entry 2 the hydroarylation reaction of phenylacetylene **1** was further conducted with different electron rich arenes **2**.

Scheme 5. Hydroarylation reaction of phenylacetylene **1** with different electron rich arenes **2** in the presence of TFA.



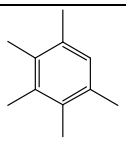
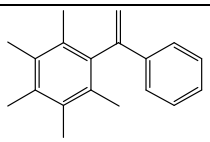
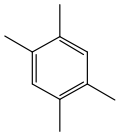
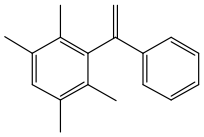
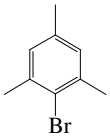
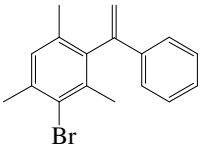
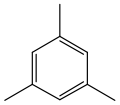
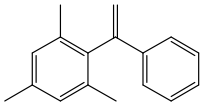
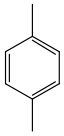
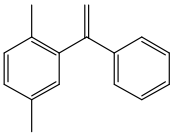
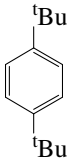
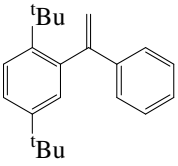
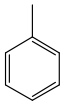
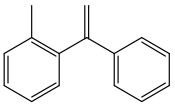
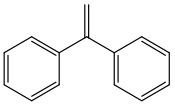
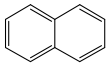
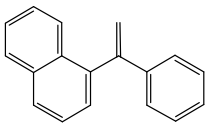
1 **2** **3** (6)

The reaction of electron rich arenes **2** such as 1,2,4,5-tetramethylbenzene **2b**, 1-bromo-2,4,6-trimethylbenzene **2c**, 1,3,5-trimethylbenzene **2d**, and 1,4-dimethylbenzene **2e** afforded 1-aryl-1-phenylethenes **3** in good to high yields (Entries 4-7). The sterically bulky 1,4-di-*tert*-butylbenzene **2f** showed low reactivity with phenylacetylene **1** and afforded the hydroarylation product **3f** in 28% yield (Entry 8). Toluene **2g**, on the other hand, reacted with phenylacetylene **1** under the same reaction conditions and gave a mixture of *ortho*-, *meta*-, and *para*-isomers **3g** in 31% yield (Entry 9). The ^{1}H NMR spectrum of the hydroarylation product of toluene showed the ratio of *ortho*-, *meta*-, and *para*-isomers was 41:9:50, indicating that this reaction was *ortho-para* directing. The *ortho* / *para* ratio (0.82) was similar to those in Friedel-Crafts alkylation reactions

of toluene with benzyl cation[8], but higher than those in electrophilic aromatic substitution reaction of tri-substituted arylvinyl cations (0.3-0.4)[9]. This high *ortho*/*para* ratio is attributable to a less steric hindrance of phenylvinyl cation compared with the trisubstituted arylvinyl cations.

Benzene **2h** and naphthalene **2i** showed a very low reactivity with phenylacetylene **1** and gave 1,1-diarylethenes **3h** and **3i** in 9 and 2% yields (Entries 10 and 11), respectively.

Table 1. Hydroarylation reaction of phenylacetylene **1** with different electron rich arenes **2** in the presence of TFA[a].

Entry	Arene **2** (mmol)	Time (h)	Product **3**	Yield (%)[b]
1	 **2a** (1)	18	 **3a**	42
2	**2a** (10)	48	**3a**	93
3	**2a** (10)	48	**3a**	65[c]
4	 **2b** (3)	24	 **3b**	75
5	 **2c** (6)	60	 **3c**	69
6	 **2d** (3)	24	 **3d**	71
7	 **2e** (10)	24	 **3e**	63
8	 **2f** (10)	60	 **3f**	28
9	 **2g** (100)	72	 **3g**	31[d,e]
10	 **2h** (100)	72	 **3h**	9[e]
11	 **2i** (5)	50	 **3i**	2

[a]***Reaction conditions***: Phenylacetylene **1**(1.0 mmol), arene **2,** TFA(1.0 mL), and CH_2Cl_2 (2.0 ml) at 30°C.

[b]Isolated yield based on phenylacetylene **1**.

[c]TFA(0.15 mL) was used.

[d]A mixture of *ortho*-, *meta*-, and *para*-isomers were formed.

[e]No CH_2Cl_2 solvent was used.

After having fruitful results from the hydroarylation reaction of phenylacetylene **1** with different arenes **2,** the hydroarylation reactions of 4-methylphenylacetylene **4**, 4-methoxyphenylacetylene **5**, and 4-fluorophenylacetylene **6** with different electron rich arenes **2** were carried out under the same reaction conditions (**Scheme 6**) as that of the reaction of phenylacetylene **1** with different arenes **2**. The results are given in **Table 2.** In the reaction of 4-methylphenylacetylene **4** with highly electron rich arenes **2a-2d,** excellent yields of the hydroarylation products **7** were obtained (Entries 1-4). However, the reaction with *p*-xylene **2e** resulted in a low yield of the product **7e** (Entry 5). Similarly, the reaction of 4-methoxyphenylacetylene **5** with electron rich arenes **2a-2d** afforded 1,1-diarylethenes **8** in high yields (Entries 6-9). A similar result was obtained in the reaction of 4-fluorophenylacetylene **6** with the arene **2a** (Entry 10).

Scheme 6. Hydroarylation reactions of alkyne **4**, **5**, or **6** with different electron rich arenes **2** in the presence of TFA.

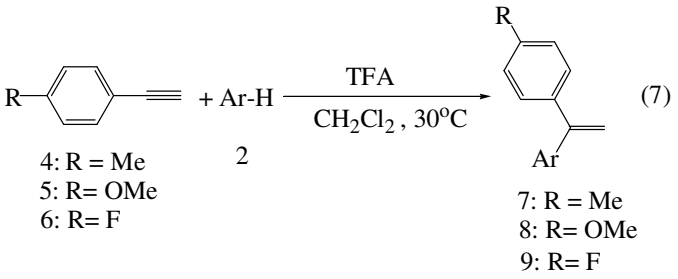
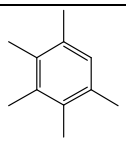
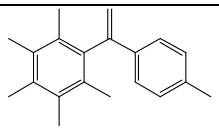
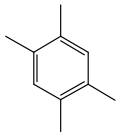
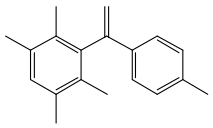
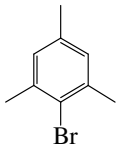
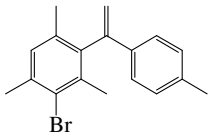
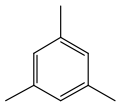
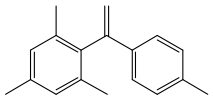
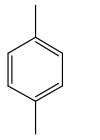
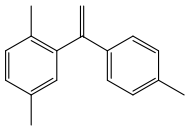
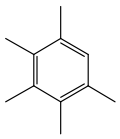
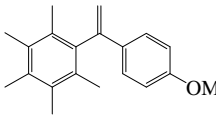
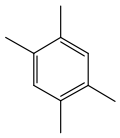
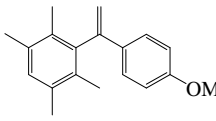
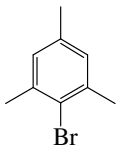
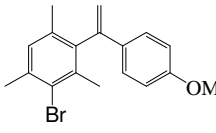
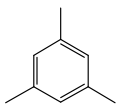
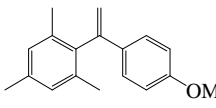
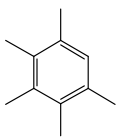
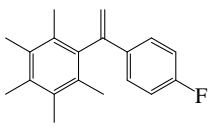


Table 2. Hydroarylation reactions of alkyne **4**, **5**, or **6** with different electron rich arenes **2** in the presence of TFA[a].

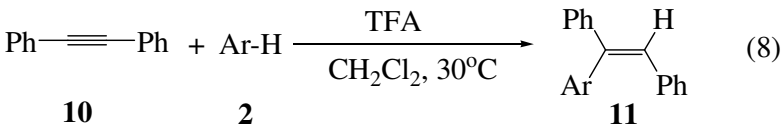
Entry	Alkyne	Arene **2**	Time (h)	Product	Yield (%)[b]
1	4	 **2a**	48	 7a	100
2	4	 **2b**	24	 7b	89
3	4	 **2c**	60	 7c	85
4	4	 **2d**	24	 7d	100
5	4	 **2e**	24	 7e	40
6	5	 **2a**	48	 8a	94
7	5	 **2b**	24	 8b	78
8	5	 **2c**	60	 8c	73
9	5	 **2d**	24	 8d	92
10	6	 **2a**	48	 9a	92

[a]***Reaction conditions***: Alkyne **4**, **5**, or **6**(1.0 mmol), arene **2**(10.0 mmol), TFA(1.0 mL), and CH_2Cl_2(2.0 mL) at 30°C.

[b]Isolated yield based on alkyne **4**, **5**, or **6**.

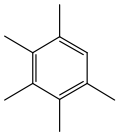
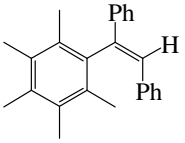
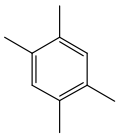
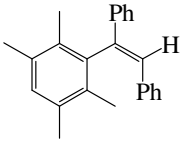
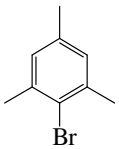
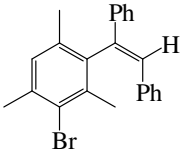
Finally, the hydroarylation reaction of the internal alkyne, diphenylacetylene **10** was examined with different electron rich arenes **2** using trifluoroacetic acid under the reaction conditions similar to the above reactions (**Scheme 7**). The results are given in **Table 3**. Diphenylacetylene **10** reacts with different electron rich arenes **2** and affords quite good yields of the desire hydroarylation products **11** (Entry 1-5). 2-Bromomesitylene **2c** gives the expected hydroarylation product **11c** in high yield as a mixture of *E*- and *Z*-isomers.

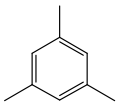
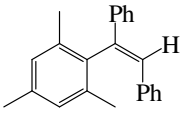
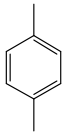
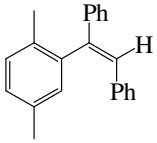
Scheme 7. Hydroarylation reaction of diphenylacetylene **10** with different electron rich arenes **2** in the presence of TFA.



10 **2** **11**

Table 3. Hydroarylation reaction of diphenylacetylene **10** with different electron rich arenes **2** in the presence of TFA[a].

Entry	Arene **2**	Time (h)	Product **11**	Yield (%)[b]
1	 **2a**	48	 11a	68
2	 **2b**	24	 11b	65
3	 **2c**	60	 11c	73[c]

4	 **2d**	24	 11d	76
5	 **2e**	24	 11e	69

[a]***Reaction conditions***: Arene **2**(10.0 mmol), diphenylacetylene **10**(1.0 mmol), TFA(1.0 mL), CH_2Cl_2(2.0 mL) at 30°C.

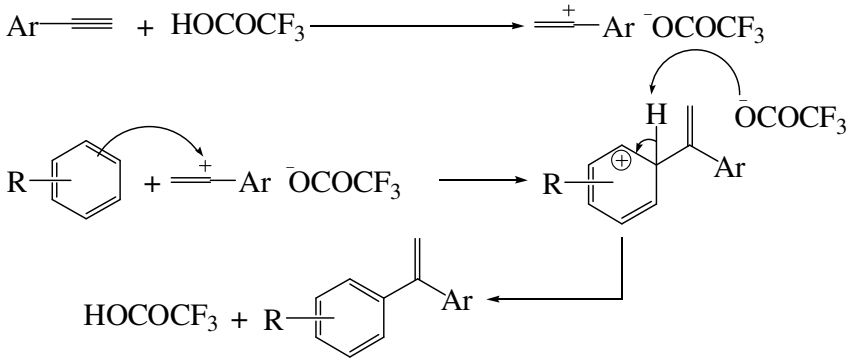
[b]Isolated yield based on diphenylacetylene **10**.

[c]A mixture of *E*- and *Z*- isomers.

4.2.1. *Possible mechanism of the TFA catalyzed hydroarylation reaction*

The hydroarylation reaction between arenes and arylsubstituted alkynes in the presence of trifluoroacetic acid are considered to procced through the formation of α-arylvinyl cations formed by the protonation of arylalkynes (**Scheme 8**). The resulting α-arylvinyl cations are stable enough to react with electron rich arenes and undergo electrophilic aromatic substitution reaction to give the desire hydroarylation product[9]. Since α-arylvinyl cations without β-substituents predominantly undergo deprotonation, the corresponding vinyl derivatives are not good choice of the substrates. Therefore, the protonation tool using arylacetylene is suitable for the synthesis of arylalkenes with hydroarylation.

Scheme 8. Mechanism of the TFA catalyzed hydroarylation reaction of alkynes



In summary, the author has demonstrated that the metal-free hydroarylation reaction of alkynes proceeds smoothly and efficiently in the presence of trifluoroacetic acid (TFA) without the involvement of transition metals or additives, when arylsubstituted alkynes and electron rich arenes are used. The simplicity of this procedure along with the mildness is practical as a synthetic tool of arylalkenes. Furthermore, this metal-free hydroarylation reaction of alkynes is particularly attractive in the pharmaceutical fields.

4.3. Experimental Section

General

All solvents and starting materials were used as received without further purification unless otherwise indicated. ^{1}H NMR, ^{13}C NMR and GC-Mass were recorded on a JEOL JNM-Al-300FT-NMR spectrometer in $CDCl_3$ solution (TMS as an internal standard) and SHIMADZU GCMS-QP5050, respectively. Melting points of the pure compounds were recorded by a YANACO melting point apparatus and are uncorrected. Column chromatographic separations were carried out using silica gel as the stationary phase. Precoated plates (silica gel $60F_{254}$, MERCK, on aluminium foils) were used for the TLC examination. Elemental analysis was performed by the Service Center of the Elemental Analysis of Organic Compounds, Faculty of Science, Kyushu University, Fukuoka, Japan.

General procedure for the hydroarylation of alkynes

In a quick-fit test tube required molar amount of arene was dissolved in 2.0 mL of dichloromethane. In the arene solution 1.0 mmol of alkyne was added. The reaction mixture was then stirred for about 5 minutes in an ice-water bath and then 1.0 mL of trifluoroacetic acid was gradually added with constant stirring. The reaction mixture was stirred for about 15 minutes in the ice-water bath and stirred again for about 15 minutes at room temperature. The temperature of the reaction mixture was then gradually increased at 30°C and stirred until the completion of the reaction. After completion of the reaction the reaction mixture was dissolved in 20.0 mL of dichloromethane and then 20.0 mL of water was added into the dichloromethane solution. Solid $NaHCO_3$ was gradually added into the reaction

mixture to neutralize the unreacted trifluoroacetic acid. The neutral aqueous reaction mixture was extracted with dichloromethane (4 x 10.0 mL) and dried over anhydrous sodium sulfate. Finally, dichloromethane was removed under reduced pressure below 40°C**.** Individual pure compounds were isolated from the reaction mixture by column chromatography using silica gel as a stationary phase.

1-(Pentamethylphenyl)-1-phenylethene **3a**[10]

Yield: 0.2541g (93%); white crystalline solid, Mp 71.9-73.9°C**.**

^{1}H NMR (300 MHz, $CDCl_3$)**:** δ =7.24-7.31(m, 5H, Ar-H), 2.10(s, 6H, 2xMe), 2.24(s, 6H, 2xMe), 2.29(s, 3H, Me), 5.07(d, 1H, vinyl-H, *J* =1.5 Hz), 5.97(d, 1H, vinyl-H, *J* =1.5 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ =148.65, 140.03, 138.71, 133.71, 132.33, 131.57, 128.35, 127.41, 126.01, 114.29, 17.84, 16.77, 16.56.

MS(EI): m/z =250 (M^+).

1-Phenyl-1-(2,3,5,6-tetramethylphenyl)ethene **3b**

Yield: 0.2241g (75%); white crystalline solid, Mp 68.2 - 69.4°C.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.22-7.29(m, 5H, Ar-H), 6.97(s, 1H, Ar-H), 5.98(d, 1H, vinyl-H, *J* =1.5 Hz), 5.07(d, 1H, vinyl-H, *J* =1.5 Hz), 2.25(s, 6H, 2xMe), 2.04(s, 6H, 2xMe).

^{13}C NMR (75 MHz, $CDCl_3$): δ =148.04, 141.08, 139.78, 133.53, 131.97, 130.29, 128.37, 127.48, 125.95, 114.19, 20.14, 16.65.

Anal. Calcd. for $C_{18}H_{20}$: C, 91.47; H, 8.53. Found: C, 91.41; H, 8.59.

1-(3-Bromo-2,4,6-trimethylphenyl)-1-phenylethene **3c**[2e]

Yieled: 0.2198g (69%). colorless viscous liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.24-7.31(m, 5H, Ar-H), 7.00(s, 1H, Ar-H), 5.98 (d, 1H, vinyl-H, *J* =1.4 Hz), 5.07(d, 1H, vinyl-H, *J* =1.4 Hz), 2.42(s, 3H, Me), 2.27(s, 3H, Me), 2.07(s, 3H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ =147.07, 139.97, 138.97, 136.83, 136.14, 134.91, 129.61, 128.50, 127.78, 125.81, 125.45, 114.81, 23.95, 21.42, 19.91.

1-Phenyl-1-(2,4,6-trimethylphenyl)ethene **3d**[2e]

Yield: 0.1705g (71%); colorless liquid**.**

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.24-7.28(m, 5H, Ar-H), 6.91(s, 2H, Ar-H), 2.11(s, 6H, 2xMe), 2.32(s, 3H, Me), 5.96(d, 1H, vinyl-H, *J* =1.5 Hz), 5.10(d, 1H, vinyl-H, *J* =1.5 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ =146.89, 139.57, 138.17, 136.41, 136.12, 128.39, 128.10, 127.51, 125.82, 114.50, 21.02, 20.06.

1-(2,5-dimethylphenyl)-1-phenylethene **3e**[2e]

Yield: 0.1376 g (63%); colorless liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.23-7.28(m, 5H, Ar-H), 7.065-7.068(m, 2H, Ar-H), 7.02-7.04(m, 1H, Ar-H), 5.18(d, 1H, vinyl-H, *J* =1.5 Hz), 5.75(d, 1H, vinyl- H, *J* =1.5 Hz), 2.34(s, 3H, Me), 2.01(s, 3H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ =149.58, 141.47, 140.68, 135.03, 132.93, 130.65, 129.96, 128.29, 128.17, 127.49, 126.50, 114.62, 20.89, 19.58.

1-(2,5-Di-tert-butylphenyl)-1-phenylethene **3f**

Yield: 0.1010g (28%); white crystalline solid, Mp 76.2-78.9°C.

^{1}H NMR (300 MHz, $CDCl_3$): δ =1.22(s, 9H, *t*-Bu), 1.32(s, 9H, *t*-Bu), 5.22(d, 1H, vinyl-H, *J* =1.5Hz), 5.90(d, 1H, vinyl-H, *J* =1.5Hz), 7.05(d, 1H, Ar-H, *J* =2.4Hz), 7.21-7.33(m, 6H, Ar-H), 7.43(d, 1H, Ar-H, *J* = 8.4 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ =151.67, 147.80, 144.80, 141.58, 139.64, 130.24, 128.17, 127.32, 126.89, 126.48, 123.98, 114.93, 36.19, 34.05, 32.26, 31.31.

Anal. Calcd. for $C_{22}H_{28}$: C, 90.35; H, 9.65. Found: C, 90.47; H, 9.67.

1-Pheny-1-tolylethene **3g**[11]

Yield: 0.0650g (31%); colorless liquid; mixture of *ortho*-, *meta*-, and *para*-isomers (41:9:50).

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.13-7.34(m, Ar-H), 5.20(d, 1H, vinyl-H, *J* =1.2 Hz), 5.41(d, 1H, vinyl-H , *J* =1.2 Hz), 5.44(d, 1H, vinyl-H, *J* =1.2Hz), 5.77(d, 1H, vinyl-H, *J* =1.2Hz), 2.05(s, 3H, *ortho*-Me), 2.34(s, 3H, *meta*-Me), 2.37(s, 3H, *para*-Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ =149.92, 149.47, 141.69, 141.62, 140.58, 138.61,

137.44, 136.08, 130.05, 129.99, 128.92, 128.84, 128.44, 128.30, 128.27, 128.13, 128.09, 127.60, 127.53, 127.51, 126.46, 125.65, 125.43, 114.79, 114.07, 113.57, 21.39, 21.13, 20.07.

MS(EI): m/z =194(M^+).

***1,1-diphenylethene* 3h**[12]

Yield: 0.0208g (9%); colorless liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.30-7.36(m, 10H, 2xAr-H), 5.46(s, 2H, vinyl-H).

***1-(1-Naphthyl)-1-phenylethene* 3i**[11c]

Yield: 0.0067g (2 %); pale yellow colored crystalline solid, Mp 46.5-48.2°C.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.21-7.91(m, 12H, Ar-H), 5.98(d, 1H, vinyl-H, *J* =1.5 Hz), 5.39(d, 1H, vinyl-H, *J* =1.5 Hz).

***1-(4-Methylphenyl)-1-(pentamethylphenyl)ethene* 7a**

Yield: 0.2696 g (100%); white crystalline solid, Mp 86.4-86.9°C.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.17(d, 2H, Ar-H , *J* =8.4 Hz), 7.06(d, 2H, Ar-H, *J* =8.4 Hz), 2.10(s, 6H, 2xMe), 2.23(s, 6H, 2xMe), 2.29(s, 3H, Me), 2.32(s, 3H, Me), 5.00(d, 1H, vinyl-H, *J* =1.5 Hz), 5.93(d, 1H, vinyl-H, *J* =1.5 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ =148.38, 138.85, 137.22, 137.16, 133.60, 132.29, 131.55, 129.07, 125.89, 113.33, 21.11, 17.83, 16.76, 16.55.

Anal. Calcd. for $C_{20}H_{24}$: C, 90.85; H, 9.15. Found: C, 90.78; H, 9.25.

***1-(4-Methylphenyl)-1-(2,3,5,6-tetramethylphenyl)ethene* 7b**

Yield: 0.2272 g (89%); white crystalline solid, Mp 117.4-117.9°C.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.16(d, 2H, Ar-H, *J* =8.1 Hz), 7.06(d, 2H, Ar-H, *J* =8.1 Hz), 6.96(s, 1H, Ar-H), 2.04(s, 6H, 2xMe), 2.24(s, 6H, 2xMe), 2.32(s, 3H, Me), 5.00(d, 1H, vinyl-H, *J* =1.5 Hz), 5.94(d, 1H, vinyl-H, *J* =1.5 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ =147.77, 141.21, 137.30, 136.90, 133.47, 131.96, 130.18, 129.09, 125.82, 113.22, 21.11, 20.15, 16.64.

Anal. Calcd. for $C_{19}H_{22}$: C, 91.14; H, 8.86. Found: C, 91.08; H, 8.90.

***1-(3-Bromo-2,4,6-trimethylphenyl)-1-(4-methylphenyl)ethene* 7c**[2e]

Yield: 0.2710 g (85%); colorless viscous liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.13(d, 2H, Ar-H, *J* = 8.1 Hz), 7.06(d, 2H, Ar-H, *J* =8.1 Hz), 6.99(s, 1H, Ar-H), 2.06(s, 3H, Me), 2.26(s, 3H, Me), 2.32(s, 3H, Me), 2.42(s, 3H, Me), 5.00(d, 1H, vinyl-H, *J* =1.2 Hz), 5.93(d, 1H, vinyl-H, *J* =1.2 Hz).
^{13}C NMR (75 MHz, $CDCl_3$): δ =146.80, 140.12, 137.64, 136.69, 136.11, 136.09, 134.90, 129.55, 129.21 125.68, 125.40, 113.82, 23.96, 21.39, 21.12, 19.89.

1-(4-Methylphenyl)-1-(2,4,6-trimethylphenyl)ethene **7d**[2e]

Yield: 0.2434 g (100%); colorless viscous liquid**.**

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.15(d, 2H, Ar-H, *J* =8.4 Hz), 7.06(d, 2H, Ar-H, *J* =8.4 Hz), 6.91(s, 2H, Ar-H), 2.32(s, 6H, 2xMe), 2.11(s, 6H, 2xMe), 5.03(d, 1H, vinyl-H, *J* =1.5 Hz), 5.91(d, 1H, vinyl-H, *J* =1.5 Hz).
^{13}C NMR (75 MHz, $CDCl_3$): δ =146.58, 138.31, 137.33, 136.65, 136.30, 136.10, 129.10, 128.02, 125.69, 113.54, 21.11, 21.03, 20.04.

1-(2,5-Dimethylphenyl)-1-(4-methylphenyl)ethene **7e**[2e]

Yield: 0.0895g (40%); colorless viscous liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.14-7.20(m, 2H, Ar-H), 7.03-7.10(m, 5H, Ar-H), 2.33(s, 6H, 2xMe), 2.01(s, 3H, Me), 5.12(d, 1H, vinyl-H, *J* =1.5 Hz), 5.72(d, 1H, vinyl-H, *J* =1.5 Hz).
^{13}C NMR (75 MHz, $CDCl_3$): δ =149.30, 141.62, 137.79, 137.28, 134.96, 132.91, 130.60, 129.89, 128.99, 128.07, 126.36, 113.72, 21.11, 20.89, 19.57.

1-(4-Methoxyphenyl)-1-(pentamethylphenyl)ethene **8a**[13]

Yield: 0.2687 g (94%); white crystalline solid, Mp 102.2-103.7^{o}C.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.25-7.20(m, 2H, Ar-H), 6.82-6.77(m, 2H, Ar-H), 5.85(d, 1H, vinyl-H, *J* =1.2 Hz), 4.95(d, 1H, vinyl-H, *J* =1.2 Hz), 3.78(s, 3H, OMe), 2.28(s, 3H, Me), 2.23(s, 6H, 2xMe), 2.10(s, 6H, 2xMe).
^{13}C NMR (75 MHz, $CDCl_3$): δ =159.09, 147.93, 138.91, 133.58, 132.67, 132.29, 131.51, 127.20, 113.66, 112.23, 55.19, 17.78, 16.75, 16.55.

1-(4-Methoxyphenyl)-1-(2,3,5,6-tetramethylphenyl)ethene **8b**

Yield: 0.2149 g (78%); white crystalline solid, Mp 124.3-126.3^{o}C.

^{1}H NMR (300 MHz, $CDCl_3$): δ=7.23-7.18(m, 2H, Ar-H), 6.96(br. s, 1H, Ar-H), 6.82-6.77(m, 2H, Ar-H), 5.86(d, 1H, vinyl-H, *J* =1.2 Hz), 4.94(d, 1H, vinyl-H, *J* =1.2 Hz), 3.78 (s, 3H, OMe), 2.24(s, 6H, 2xMe), 2.04(s, 6H, 2xMe)..

^{13}C NMR (75 MHz, $CDCl_3$): δ =159.15, 147.35, 141.29, 133.48, 132.43, 131.91, 130.16, 127.14, 113.70, 112.10, 55.21, 20.13, 16.58.

Anal. Calcd. for $C_{19}H_{22}O$: C, 85.67; H, 8.32. Found: C, 85.57; H, 8.43.

1-(2-Bromo-2,4,6-trimethylphenyl)-1-(4-methoxyphenyl)ethene **8c**[2e]

Yield: 0.2434 g (73%); colorless viscous liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ=7.21-7.16(m, 2H, Ar-H), 6.99(br. s, 1H, Ar-H), 6.82 - 6.77(m, 2H, Ar-H), 2.41(s, 3H, Me), 2.27(s, 3H, Me), 2.07(s, 3H, Me), 5.85 (d, 1H, vinyl-H, *J* =1.5 Hz), 4.95(d, 1H, vinyl-H, *J* =1.5 Hz), 3.78(s, 3H, OMe).

^{13}C NMR (75 MHz, $CDCl_3$): δ =159.36, 146.39, 140.22, 136.68, 136.08, 134.87, 131.59, 129.57, 127.03, 125.41, 113.83, 112.69, 55.23, 23.93, 21.34, 19.84.

1-(4-Methoxyphenyl)-1-(2, 4, 6-trimethylphenyl)ethene **8d**[2e]

Yield: 0.2424 g (92%); colorless viscous liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.22-7.17(m, 2H, Ar-H), 6.90(br. s, 2H, Ar-H), 6.82 -6.77(m, 2H, Ar-H), 3.78(s, 3H, OMe), 2.31(s, 3H, Me), 2.11(s, 6H, 2xMe), 5.84(d, 1H, vinyl-H, *J* =1.2 Hz), 4.98(d, 1H, vinyl-H, *J* =1.2 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ =159.17, 146.16, 138.38, 136.28, 136.06, 132.17, 128.03, 127.00, 113.71, 112.42, 55.21, 21.02, 19.99.

1-(4-Fluorophenyl)-1-(pentamethylphenyl)ethene **9a**

Yield: 0.2905 g (92%); white crystalline solid, Mp 77.6-78.8^{o}C.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.25[dd, 2H, Ar-H, *J* =5.1 (F-H^{meta}) and 9.0 Hz], 6.93[dd, 2H, Ar-H, *J* =9.0 (F-H^{ortho}) and 9.0 Hz], 5.89(s, 1H, Vinyl-H), 5.03(s, 1H, vinyl-H), 2.28(s, 3H, Me), 2.23(s, 6H, 2xMe), 2.09(s, 6H, 2xMe).

^{13}C NMR (75 MHz, $CDCl_3$): δ =162.36(d, $^1J_{C\text{-}F}$ =246.0 Hz), 147.61, 138.48, 136.15(d, $^4J_{C\text{-}F}$ =3.0 Hz), 133.86, 132.43, 131.44, 127.65(d, $^3J_{C\text{-}F}$ =8.0 Hz), 115.16(d, $^2J_{C\text{-}F}$ =21.0 Hz), 113.95, 17.77, 16.75, 16.54.

Anal. Calcd. for $C_{19}H_{21}F$: C, 85.03; H, 7.89. Found: C, 85.29; H, 7.97.

(Z)-1-(Pentamethylphenyl)-1,2-diphenylethene **11a**[10]

Yield: 0.2234 g (68%); white crystalline solid, Mp 112.8-115.5°C.

^{1}H NMR (300 MHz, $CDCl_3$): δ =6.91-7.35(m, 11H, Ar-H & vinyl-H), 2.31(s, 3H, Me), 2.21(s, 6H, 2xMe), 2.01(s, 6H, 2xMe).

^{13}C NMR (75 MHz, $CDCl_3$): δ =142.18, 141.67, 137.60, 136.24, 133.90, 132.72, 131.08, 128.59, 128.35, 128.13, 127.82, 127.09, 126.71, 126.18, 17.20, 16.89, 16.65.

(Z)-1,2-Diphenyl-1-(2,3,5,6-tetramethylphenyl)ethene **11b**

Yield: 0.2023g (65%); white crystalline solid, Mp 87.9-90.1°C.

^{1}H NMR (300 MHz, $CDCl_3$): δ =6.90-7.34(m, 12H, Ar-H & vinyl-H), 2.23(s, 6H, 2xMe), 1.95(s, 6H, 2xMe).

^{13}C NMR (75 MHz, $CDCl_3$): δ =141.78, 140.95, 138.85, 137.48, 134.00, 131.72, 130.69, 128.55, 128.40, 128.17, 127.83, 127.20, 126.83, 126.11, 20.22, 16.09.

Anal. Calcd. for $C_{24}H_{24}$: C, 92.26; H, 7.74. Found: C, 92.19; H, 7.80.

1-(3-Bromo-2,4,6-trimethylphenyl)-1,2-diphenylethene **11c**

Yield: 0.2784 g (73%); mixture of *E*- and *Z*-isomers (44:46), colorless semi-solid.

^{1}H NMR (300 MHz, $CDCl_3$): δ =6.92-7.30(m, 23H, Ar-H & vinyl-H), 6.48(s, 1H, vinyl-H), 2.45(s, 3H, Me), 2.43(s, 3H, Me), 2.40(s, 3H, Me), 2.20(s, 6H, 2xMe), 1.95(s, 3H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ =142.43, 140.99, 140.81, 139.55, 138.66, 137.87, 137.25, 137.00, 136.87, 136.19, 135.00, 134.89, 130.65, 130.28, 129.76, 129.54, 129.21, 128.71, 128.54, 128.44, 128.31, 128.16, 128.05, 127.47, 127.23, 127.21, 126.96, 125.96, 125.84, 125.63, 24.10, 23.97, 21.72, 20.90, 20.22, 19.61.

MS(EI): m/z =376[M^+] / 378 [M + 2].

Anal. Calcd. for $C_{23}H_{21}Br$: C, 73.21; H, 5.61. Found: C, 73.09; H, 5.57.

(Z)-1,2-Diphenyl-1-(2,4,6-trimethylphenyl)ethene **11d**[2j]**.**

Yield: 0.2300 g (76%); white crystalline solid, Mp 138.8-140.9°C.

^{1}H NMR (300 MHz, $CDCl_3$): δ =6.92-7.34(m, 13H, Ar-H & vinyl-H), 2.35(s, 3H, Me), 2.00(s, 6H, 2xMe).

^{13}C NMR (75 MHz, $CDCl_3$): δ =141.51, 139.79, 137.47, 136.86, 136.03, 135.89, 128.70, 128.44, 128.42, 128.21, 128.05, 127.27, 126.94, 125.99, 21.19, 19.80.

***(Z)-1-(2,5-Dimethylphenyl)-1,2-diphenylethene* 11e[2j].**

Yield: 0.1967 g (69 %); colorless viscous liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ =6.94-7.34(m, 14H, Ar-H & vinyl-H), 2.27(s, 3H, Me), 1.99(s, 3H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ =142.45, 141.36, 139.45, 137.35, 135.76, 133.27, 130.46, 130.36, 128.96, 128.36, 128.30, 128.08, 127.97, 127.28, 126.83, 126.60, 20.97, 19.09.

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CHAPTER 5

Iodoarylation of Arylsubstituted Alkynes with Molecular Iodine in the Presence of Hypervalent Iodine Reagents

A Very Convenient, Simple Procedure for Arylsubstituted Iodoalkenes from Simple Arenes

5.1. Introduction

Direct catalytic functionalization of **C-H** bond of simple arenes via the formation of new **carbon-carbon** bond between arenes and olefins has received significant attention. The process provides a direct synthesis of various functionalized aromatic compounds bearing conjugated **carbon-carbon** bonds from the simple arenes in one step, being the useful alternative of Heck-type coupling reactions of aromatic halides and olefins. To date, various methods for the direct functionalization of arenes via the formation of new **carbon-carbon** bond between simple arenes and olefins have been developed, which were catalyzed by transition metals or Lewis acid[1]. Although such metal-catalyzed **carbon-carbon** bond formation methods are excellent, efficient and very powerful, but there are some limitations, for instance, in many cases poor regioselectivity, special caution for handling metal catalysts under inert atmosphere and to carry out the reaction using transition metal catalysts requires activated substrates or strong acidic or forcing conditions.

Besides these, contamination of pharmaceutical materials with a trace amount of transition metals in the processes of manufacture causes a serious problem. These drawbacks of the direct formation of **carbon-carbon** bond between simple arenes and olefins using transition metal catalysts have attracted the attention to develop a more convenient and simple new synthetic method for the direct functionalization of arenes through the formation of new **carbon-carbon** bond without using any transition metal catalysts.

In the present study, an attempt has been made to use molecular iodine for the direct formation of **carbon-carbon** bond between arenes and alkynes to replace the metal salts so that it can avoid the use of the heavy metals.

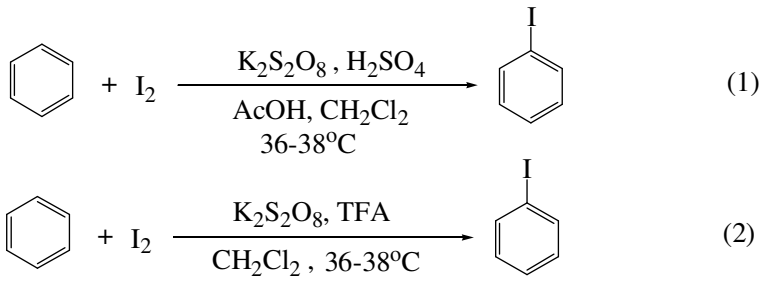
In recent years, a large number of organic reactions have been investigated using molecular iodine-catalyzed and molecular iodine-induced methods. Iodine is an inexpensive weak Lewis acid, non-toxic, natural friendliness and readily available reagent for various organic transformations and yields products with outstanding

selectivity with minimum by products. Moreover, iodine is volatile and it is very easy to remove from the reaction medium.

The reactivity of molecular iodine towards the addition reaction is very low because of the low electrophilic property of molecular iodine. In the presence of an appropriate oxidizing agent molecular iodine can behave as a powerful electrophile.

Very recently, Kitamura *et al* reported that the direct iodination of aromatic compounds with molecular iodine proceeds smoothly in the presence of potassium peroxodisulfate (**$K_2S_2O_8$**) as an oxidant and gives iodoarenes in good yields (**Scheme 1**)[2].

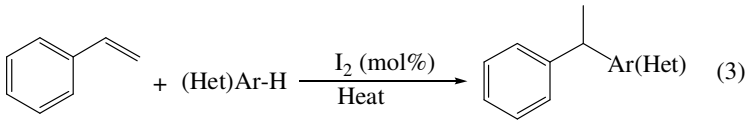
Scheme 1



This direct iodination reaction initiated to extend the iodination reaction of arenes to iodoarylation reaction of alkynes with arenes for the direct formation of new **carbon-carbon** bonds. It was assumed that an alkyne would be activated by molecular iodine to form a bridged iodonium ion which would then undergo electrophilic aromatic substitution reaction with an arene to give the desire iodoarylation products.

Very recently, Yao *et al* reported that molecular iodine mediates the hydroarylation reaction of styrenes with arenes and heteroarenes in the absence of solvent and transition metals to afford 1,1-diarylalkanes in good to high yields (**Scheme 2**)[3].

Scheme 2



(3)

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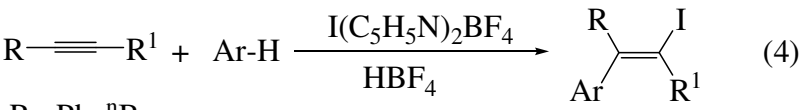
Literature survey shows that the iodoarylation reaction of alkynes with arenes using molecular iodine has not yet been reported in the literature.

Barluenga *et al* reported the intermolecular iodoarylation reaction of alkynes with arenes using bis(pyridine)iodonium(**I**)tetrafluoroborate (**IPy_2BF_4**) as an iodonium ion source[4]. According to their report alkynes react with bis(pyridine)iodonium(**I**)tetrafluoroborate(**IPy_2BF_4**) and arenes in a Friedel-Crafts type alkylation reaction to give, in a regio- and stereoselective way, *trans*-β-iodostyrene derivatives (**Scheme 3**).

Scheme 3



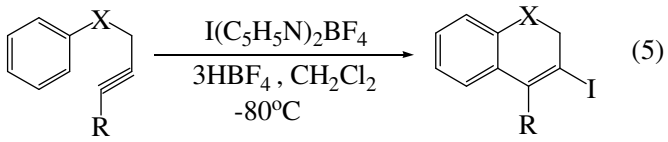
(4)

R= Ph, ^{n}Bu

R^1 = H , Me

Barluenga *et al* further reported the intramolecular iodoarylation reaction of alkynes using the same bis(pyridine)iodonium(**I**) tetrafluoroborate (**IPy_2BF_4**) as an iodonium ion source[5]. The intramolecular iodoarylation reaction of heteroatom-tethered ω-arylalkynes in the presence of iodonium ion source bis(pyridine)iodonium(**I**)tetrafluoroborate(**IPy_2BF_4**) offers an efficient and straightforward entry to heterocycles (**Scheme 4**). As a result, both **carbon-carbon** ring-closing from readily available precursors and concomitant selective iodination takes place.

Scheme 4



(5)

X= O, NTs , NMs

Although the bis(pyridine)iodonium(**I**) tetrafluoroborate (**IPy_2BF_4**) is an effective and powerful reagent for the iodoarylation of alkynes, but it is very expensive, and toxic mercury oxide is required to prepare this reagent[6]. Therefore, it is desirable to seek a convenient, safe, cheap, non-toxic, environmentally friendly and readily available simple iodine reagent for the formation of new **carbon-carbon** bond through the iodoarylation reaction of alkynes.

Literature survey shows that till now the use of molecular iodine in the presence of **$PhI(OAc)_2$** or other hypervalent iodine reagents for the formation of **carbon-carbon** bond between arenes and alkynes through the iodoarylation reaction has not attracted the attention of the chemists.

In this chapter, a more convenient and very simple **carbon-carbon** bond formation method between electron rich arenes and aryl substituted alkynes using molecular iodine in the presence of hypervalent iodine reagents is reported.

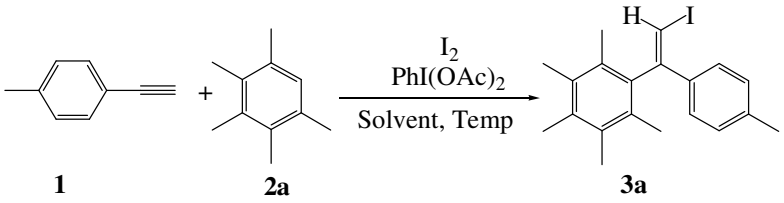
5.2. Results and Discussion

Iodoarylation reaction of alkynes is accompanied by the generation of proton and competes with the protonation of alkynes. The iodoarylation reaction of *p*-methylphenylacetylene **1** with pentamethylbenzene **2a** using **$I_2/K_2S_2O_8$** reagent system was found to produce a hydroarylation product as a by-product along with the desired iodoarylation product. The contamination of the iodoarylation product with the inseparable hydroarylation by-product causes many difficulties in the separation and purification processes. (Diacetoxyiodo)benzene, **$PhI(OAc)_2$** is an appropriate oxidizing agent that has both the functions of converting molecular iodine into iodonium ion and of receiving proton with the acetate ion. Moreover,

PhI(OAc)$_2$ is one of the most commercially available hypervalent iodine compound and has been widely used in organic synthesis.

Direct preparation of 1,1-diaryl-2-iodoethenes was carried out from the corresponding electron rich arenes and aryl-substituted alkynes using molecular iodine in the presence of hypervalent iodine reagent, **PhI(OCOPh)$_2$** in CH_3CN solvent at 82^oC. In the present study, to optimize the iodoarylation reaction initially, the research work was concentrated on the efficiency of the iodoarylation reaction of *p*-methylphenylacetylene **1** with electron rich arene, pentamethylbenzene **2a** in the presence of molecular iodine and **PhI(OAc)$_2$** (**Scheme 5**).

Scheme 5. The iodoarylation reaction of *p*-methylphenylacetylene **1** with pentamethylbenzene **2a** in the presence of molecular iodine and **PhI(OAc)$_2$**.



(6)

5.2.1. Optimization of the reaction conditions

To optimize the reaction conditions the reaction of *p*-methylphenylacetylene **1** and pentamethylbenzene **2a** in the presence of molecular iodine and **PhI(OAc)$_2$** was explored under different reaction conditions. The results are given in **Table 1**.

Table 1. Optimization of the reaction conditions for the reaction of *p*-methyl-phenylacetylene **1** and pentamethylbenzene **2a** in the presence of **I$_2$** and **PhI(OAc)$_2$**[a].

Entry	**2a** (mmol)	$PhI(OAc)_2$ (mmol)	Solvent (mL)	Temp. (^oC)	Time (h)	Yield of **3a** (%)[b]
1	1	1.25	$(CH_2)_2Cl_2$ (2mL)	45	28	12
2	5	3	CH_3CO_2H (2mL)	60	48	23
3	1.5	3	MeCN (2 mL)	60	48	31
4	5	3	MeCN (2 mL)	60	48	52
5	5	3	MeCN (4 mL)	78	56	67
6	**10**	**3**	**MeCN (4 mL)**	**82**	**65**	**78**
7	10	3	EtOAc (4 mL)	78	65	13

[a]***Reaction conditions***: *p*-Methylphenylacetylene **1** (1.0 mmol), pentamethyl-benzene **2a, I_2**(1.25 mmol), $PhI(OAc)_2$ and solvent.

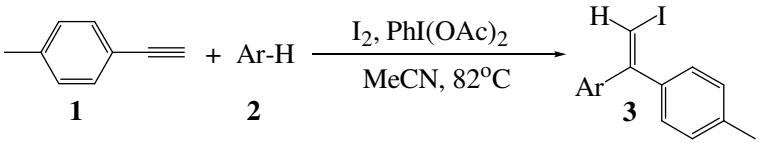
[b]Isolated yield based on *p*-methylphenylacetylene **1.**

The iodoarylation reaction was carried out in defferent solvent systems such as $(CH_2)_2Cl_2$, CH_3COOH, MeCN and EtOAc under different reaction conditions. The reaction in $(CH_2)_2Cl_2$ at 45^oC for 28 hours afforded 1-iodo-2-(pentamethylphenyl)-2-(4-methylphenyl)ethene **3a,** but the yield was very low (Entry 1). To improve the yield increasing the amount of pentamethylbenzene **2a** and **$PhI(OAc)_2$**, the reaction was further carried out using CH_3COOH, MeCN and EtOAc under different reaction conditions (Entries 2-3 and 7). The best result (31%) was obtained in the presence of solvent MeCN (Entry 3). Extension of the reaction time and at higher temperature improved the yield (78%) of the product **3a** (Entry 6). Thus, the entry 6 is the optimum condition for the reaction.

Using the reaction conditions of the Entry 6 in **Table 1** the iodoarylation reaction of *p*-methylphenylacetylene **1** was further carried out with different electron rich arenes **2**(**Scheme 6**). The results are given in **Table 2.** The reaction with mesitylene **2b**, 1,2,4,5-tetramethylbenzene **2c**, and bromomesitylene **2d** afforded the corresponding iodoarylation products **3b-3d** in moderate yields (Entries 1-3). The reaction with *p*-xylene **2e** gave very low yield (8%) of the iodoarylation product **3e** (Entry 4).

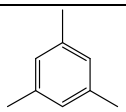
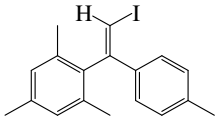
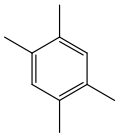
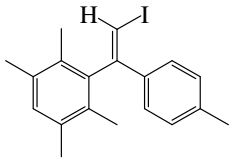
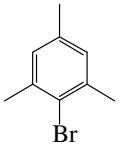
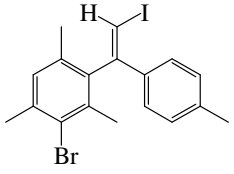
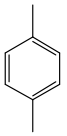
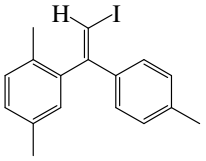
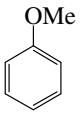
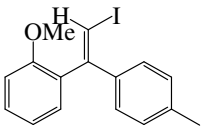
Anisole **2f**, on the other hand, reacts with *p*-methylphenylacetylene **1** under the same reaction conditions and gives a mixture of *ortho*-, *meta*-, and *para*-isomers of the iodoarylation product **3f** in 35% yield (Entry 5). The ^{1}H NMR spectrum of the iodoarylation product of anisole showed the ratio of *ortho*-, *meta*-, and *para*-isomers was (20:20:60).

Scheme 6. The iodoarylation reaction of *p*-methylphenylacetylene **1** with different electron rich arenes **2** in the presence of molecular iodine and **PhI(OAc)$_2$**.



(7)

Table 2. The iodoarylation reaction of *p*-methylphenylacetylene **1** with different electron rich arenes **2** in the presence of molecular iodine and **PhI(OAc)$_2$**[a].

Entry	Arene **2**	Time (h)	Product **3**	Yield (%)[b]
1	 2b	65	 3b	62
2	 2c	65	 3c	40
3	 2d	65	 3d	26[c]
4	 2e	65	 3e	08[c]
5	 2f	40	 3f	35[d,e]

[a]***Reaction conditions*** : Arene **2** (10.0 mmol), *p*-methylphenylacetylene **1** (1.0 mmol), I_2 (1.25 mmol), **$PhI(OAc)_2$** (3.0 mmol), CH_3CN (4.0 mL) at 82°C.

[b]Isolated yield based on *p*-methylphenylacetylene **1.**

[c]A mixture of *E*- and *Z*- isomers.

[d]A mixture of *ortho*-, *meta*-, and *para*-isomers was formed.

[e]Reaction was carried out at 70°C.

5.2.2. *Effect of different hypervalent iodine compounds on the iodoarylation reaction*

To improve the yields of the iodoarylation product **3a** the effect of different [bis(acyloxy)iodo]benzenes, [hydroxy(tosyloxy)iodo]benzene, **PhI(OH)OTs**, and silver benzoate, **AgOCOPh** were examined on the iodoarylation reaction of *p*-methylphenylacetylene **1** with electron rich arene, pentamethylbenzene **2a** (**Scheme 7**). Some [bis(acyloxy)iodo]benzenes were prepared from benzoic acid, *m*-and *p*-chlorobenzoic acid, *p*-nitrobenzoic acid, *p*- toluic acid, and *p*-anisic acid, according to the standard literature method[8]. The results are given in **Table 3**. The catalyst **$PhI(OCOPh)_2$** showed the highest activity among all other catalysts tested in the **Table 3**, giving the iodoarylation product **3a** in 86% yield (Entries 1-6). The catalyst, [bis(*p*-nitrobenzoyloxy)iodo]benzene also afforded the product **3a** in good yield (80%) (Entry 4), but the catalyst **$PhI(OCOPh)_2$** was used as the activator because of the readily availability of benzoic acid. [Hydroxy(tosyloxy)iodo]benzene(Koser's salt), **PhI(OH)OTs** and Silver benzoate, **AgOCOPh** showed a very little effect on the iodoarylation reaction (Entries 7 and 8).

Scheme 7. Effect of different hypervalent iodine compounds on the iodoarylation reaction of *p*-methylphenylacetylene **1** with pentamethylbenzene **2a**.

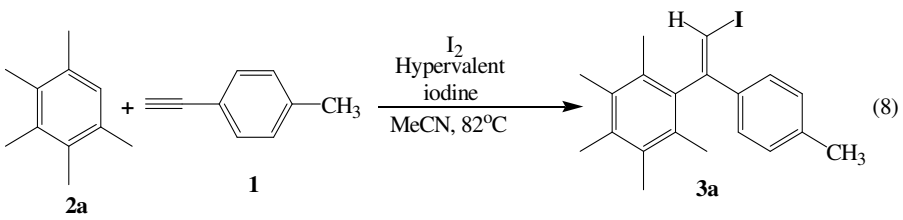
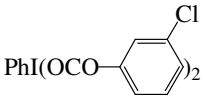
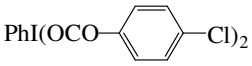
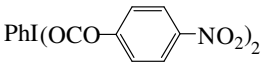
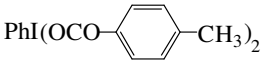
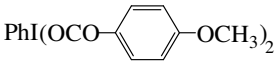


Table 3. Effect of different hypervalent iodine compounds on the iodoarylation reaction of *p*-methylphenylacetylene **1** with pentamethylbenzene **2a**[a].

Entry	Hypervalent iodine compound	Yield of **3a** (%)
1	**PhI(OCOPh)$_2$** [Bis(benzoyloxy)iodo]benzene	86
2	 [Bis(*m*-chlorobenzoyloxy)iodo]benzene	78
3	 [Bis(*p*-chlorobenzoyloxy)iodo]benzene	65
4	 [Bis(*p*-nitrobenzoyloxy)iodo]benzene	80
5	 [Bis(*p*-methylbenzoyloxy)iodo]benzene	74
6	 [Bis(*p*-methoxybenzoyloxy)iodo]benzene	70
7	PhI(OH)OTs, [Hydroxy(tosyloxy)iodo]benzene	33[b,c]
8	AgOCOPh, Silver benzoate	12[d]

[a]***Reaction conditions*:** Pentamethylbenzene **2a** (10.0 mmol), *p*-methylphenylacetylene **1** (1.0 mmol), **I_2** (1.25 mmol), catalyst (3.0 mmol), CH_3CN (6.0 mL), 82^oC and 65 hours.

[b]Iodoarylation product **3a** was contaminated with hydroarylation product.

[c]The reaction was carried out using pentamethylbenzene **2a** (3.0 mmol) in MeCN (4.0 mL) at 45^oC for 28 hours.

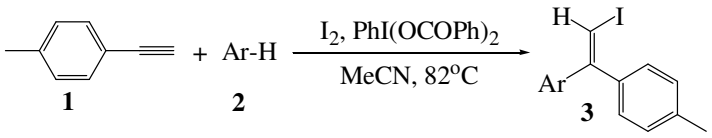
[d]The reaction was carried out using pentamethylbenzene **2a** (2.0 mmol), *p*-methylphenylacetylene **1** (1.0 mmol), I_2 (1.0 mmol), AgOCOPh (1.0 mmol) in MeCN (2.0 mL) at 40^oC for 36 hours.

5.2.3. Scope of the iodoarylation reaction using molecular iodine in the presence of PhI(OCOPh)$_2$

The iodoarylation reaction of *p*-methylphenylacetylene **1** was carried out with different electron rich arenes **2** using molecular iodine in the presence of

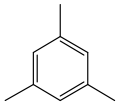
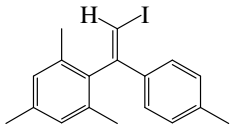
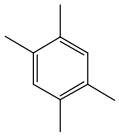
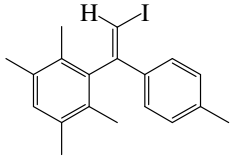
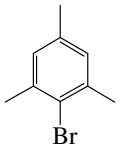
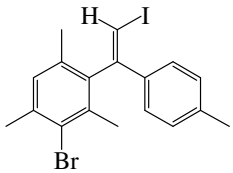
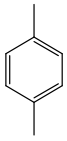
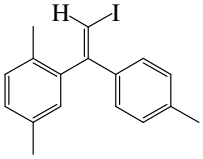
PhI(OCOPh)$_2$ (**Scheme 8** and **Table 4**). The results of the iodoarylation reaction of *p*-methylphenylacetylene **1** with various electron rich arenes **2** showed that the iodoarylation reaction gave iodoarylated products in good yields. Especially, the electron rich arene, mesitylene **2b** gave the iodoarylation product **3b** (Entry 1) in high yield (75%). The reaction with 1,2,4,5-tetramethylbenzene **2c** and bromomesitylene **2d** gave the iodoarylation product **3c** and **3d** in 56 and 42% yields, respectively (Entry 2 and 3). The reaction with moderately electron rich arene, *p*-xylene **2e** gave low yield (33%) of the iodoarylation product **3e** (Entry 4).

Scheme 8. The iodoarylation reaction of *p*-methylphenylacetylene **1** with different electron rich arenes **2** in the presence of molecular iodine and **PhI(OCOPh)$_2$**.



1 **2** **3** (9)

Table 4. The iodoarylation reaction of *p*-methylphenylacetylene **1** with different electron rich arenes **2** in the presence of molecular iodine and **PhI(OCOPh)$_2$**[a].

Entry	Arene **2**	Time (h)	Product **3**	Yield (%)[b]
1	 2b	65	 3b	75
2	 2c	67	 3c	56
3	 Br 2d	72	 Br 3d	42[c]
4	 2e	72	 3e	33[c]

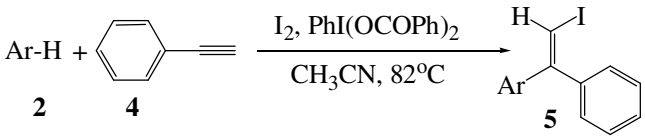
[a]***Reaction conditions*:** Arene **2**(10.0 mmol), *p*-methylphenylacetylene **1**(1.0 mmol), I_2 (1.25 mmol), $PhI(OCOPh)_2$ (3.0 mmol), CH_3CN (6.0 mL) at 82°C .

[b]Isolated yield based on *p*-methylphenylacetylene **1**.

[c]A mixture of *E*- and *Z*-isomers.

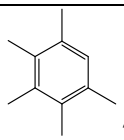
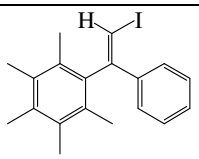
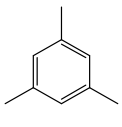
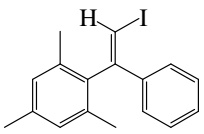
Next, the iodoarylation reaction of phenylacetylene **4** was examined with different electron rich arenes **2** under the same reaction conditions as used for the iodoarylation reaction of *p*-methylphenylacetylene **1** with different electron rich arenes **2** (**Scheme 9**). The results of the reactions are given in **Table 5**. The reaction of electron rich arenes such as pentamethylbenzene **2a**, mesitylene **2b**, and 1,2,4,5-tetramethylbenzene **2c** gave the iodoarylation products **5a-5c** in good yields (Entries 1-3). The moderately electron rich arenes such as 2-bromomesitylene **2d** and *p*-xylene **2e** showed very low reactivity with phenylacetylene **4** and gave low yields (32 and 24%) of the iodoarylation products **5d** and **5e** respectively (Entries 4-5).

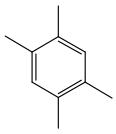
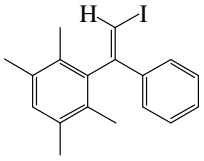
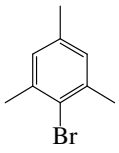
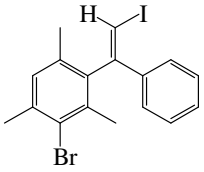
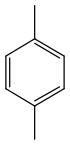
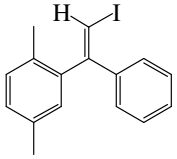
Scheme 9. The iodoarylation reaction of phenylacetylene **4** with different electron rich arenes **2** in the presence of molecular iodine and **$PhI(OCOPh)_2$**.



(10)

Table 5. The iodoarylation reaction of phenylacetylene **4** with different electron rich arenes **2** in the presence of molecular iodine and **$PhI(OCOPh)_2$**[a].

Entry	Arene **2**	Time (h)	Product **5**	Yield (%)[b]
1	 2a	65	 5a	71
2	 2b	70	 5b	61

3	 2c	73	 5c		59
4	 2d	76	 5d		32
5	 2e	72	 5e		24

[a]***Reaction conditions***: Arene **2** (10.0 mmol), phenylacetylene **4** (1.0 mmol), I_2 (1.25 mmol), $PhI(OCOPh)_2$ (3.0 mmol), CH_3CN (6.0 mL) at 82°C.

[b]Isolated yield based on phenylacetylene **4.**

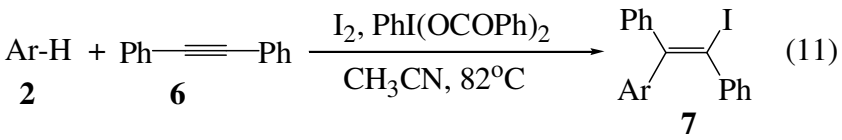
The iodoarylation reaction of arylacetylenes with arenes proceeds regio- and stereoselectively to give a single isomer of the possible *E*- and *Z*-1,1-diaryl-2-iodoethenes **3** and **5**. **NOE** experiments were conducted to determine the stereochemistry of the iodoarylation product **3a**, but only a very small enhancement (3%) of the vinylic proton was observed when *ortho* methyl proton was irradiated. This may be attributed to deviation of the pentamethylbenzene ring from the olefinic plane. Therefore, to determine the stereochemistry of the iodoarylation products **3** and **5**, the chemical shift of the vinylic protons were calculated according to the literature[7] and compared with the observed chemical shift value of the iodoarylation products **3** and **5**. The calculation of the chemical shift value concerning the vinylic proton for the iodoarylation products **3** and **5** gives 6.51 ppm for the *E*-isomer and 6.84 ppm for the *Z*-isomer. In the ^1H NMR spectra of the iodoarylation products **3** and **5**, a singlet peak of the vinylic proton was observed at the range of 6.30-6.55 ppm.

Therefore, on the basis of the calculated chemical shift value the stereochemistry of the iodoarylation products **3** and **5** is considered to be *E*. This result suggests

that the iodoarylation reaction of arylalkynes proceeds with *trans* addition. This is in accord with the results obtained by Barluenga *et al* [4].

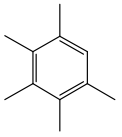
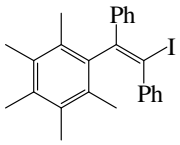
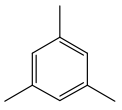
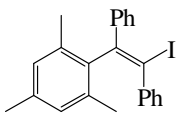
Again, the iodoarylation reaction of internal alkyne, diphenylacetylene **6** was explored with electron rich arenes **2** under the above reaction conditions (**Scheme 10**). The results of the reactions are given in **Table 6**. The reaction of electron rich arenes such as pentamethylbenzene **2a** and mesitylene **2b** with the internal alkyne, diphenylacetylene **6** yielded the expected iodoarylation products **7** in very low yields 14 and 8% (Entries 1 and 2), respectively. The low yield of the reaction may be due to steric hindrance.

Scheme 10. The iodoarylation reaction of diphenylacetylene **6** with different electron rich arenes **2** in the presence of molecular iodine and **PhI(OCOPh)$_2$.**



(11)

Table 6. The iodoarylation reaction of diphenylacetylene **6** with different electron rich arenes **2** in the presence of molecular iodine and **PhI(OCOPh)$_2$**[a].

Entry	Arene **2**	Time (h)	Product **7**	Yield (%)[b]
1	 **2a**	76	 7a	14
2	 **2b**	76	 7b	8.0

[a]***Reaction conditions*:** Arene **2** (10.0 mmol), diphenylacetylene **6** (1.0 mmol), I_2 (1.25 mmol), PhI(OCOPh)$_2$ (3.0 mmol), CH_3CN (6.0 mL) at 82°C.

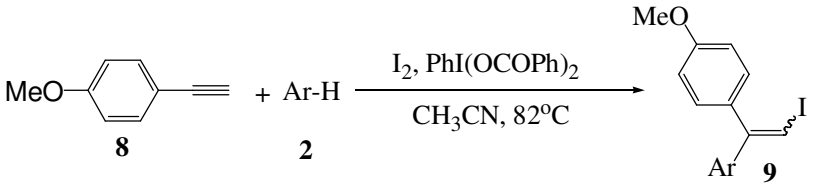
[b]Isolated yield based on diphenylacetylene **6.**

Further, the iodoarylation reaction of 4-methoxyphenylacetylene **8** was carried out with different electron rich arenes **2** under the above reaction conditions (**Scheme 11**). The results of the reactions are shown in **Table 7**. The reaction of electron

rich arenes **2a-2c** gave the iodoarylation products **9** in good yields (Entries 1-3). Bromomesitylene **2d** and *p*-xylene **2e** showed very low reactivity with 4-methoxyphenylacetylene **8** and the yields were 32 and 16 % (Entries 4 and 5), respectively.

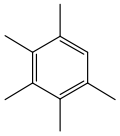
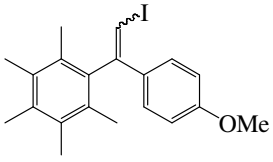
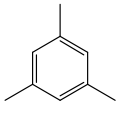
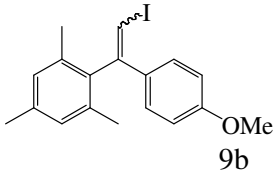
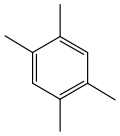
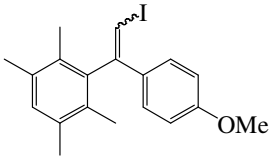
In the case of 4-methoxyphenylacetylene **8** the iodoarylation reaction completely lost its stereospecificity and gave a mixture of *E*- and *Z*-isomers of the iodoarylation products **9**. This behavior is different from that observed in the case of arylacetylenes **1** and **4.**

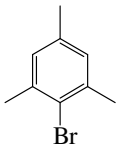
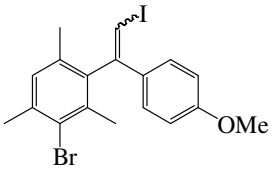
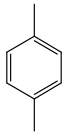
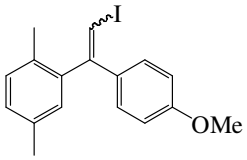
Scheme 11. The iodoarylation reaction of 4-methoxyphenylacetylene **8** with different electron rich arenes **2** in the presence of molecular iodine and **PhI(OCOPh)$_2$**.



(12)

Table 7. The iodoarylation reaction of 4-methoxyphenylacetylene **8** with different electron rich arenes **2** in the presence of molecular iodine and **PhI(OCOPh)$_2$**[a].

Entry	Arene **2**	Time (h)	Product **9**[b]	Yield (%)[c]
1	 2a	72	 9a	75
2	 2b	72	 9b	63
3	 2c	73	 9c	62

4	 2d	76	 9d	32
5	 2e	76	 9e	16

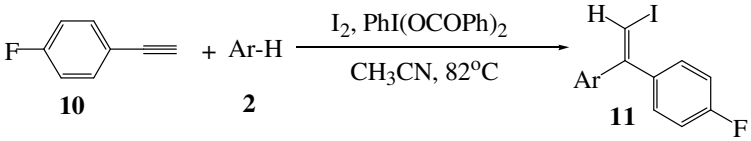
[a]***Reaction conditions*:** Arene **2** (10.0 mmol), 4-methoxyphenylacetylene **8** (1.0 mmol), I_2 (1.25 mmol), $PhI(OCOPh)_2$ (3.0 mmol), CH_3CN (6.0 mL) at 82°C.

[b]A mixture of *E*- and *Z*-isomers.

[c]Isolated yield based on 4-methoxyphenylacetylene **8.**

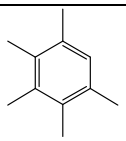
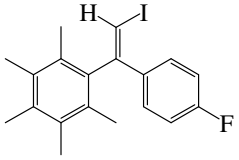
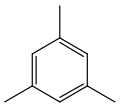
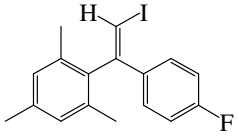
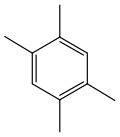
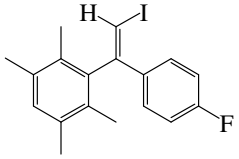
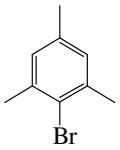
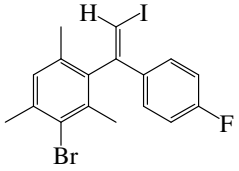
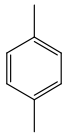
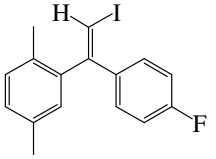
Next, the iodoarylation reaction of *p*-fluorophenylacetylene **10** was examined with various electron rich arenes **2** under the above reaction conditions (**Scheme 12**). The results of the reactions are shown in **Table 8**. The reaction of electron rich arenes **2a-2c** gave the iodoarylation products **11** in good yields (Entries 1-3). The moderately electron rich arenes such as bromomesitylene **2d** and *p*-xylene **2e** showed very low reactivity with *p*-fluorophenylacetylene **10** and the yields were 27 and 23%, respectively (Entries 4 and 5). *p*-Fluorophenylacetylene **10** showed the similar behavior of the alkynes, *p*-methylphenyacetylene **1** and phenylacetylene **4**, and underwent stereospecific iodoarylation reaction.

Scheme 12. The iodoarylation reaction of *p*-fluorophenylacetylene **10** with different electron rich arenes **2** in the presence of molecular iodine and **$PhI(OCOPh)_2$**.



10 **2** **11** (13)

Table 8. The iodoarylation reaction of *p*-fluorophenylacetylene **10** with different electron rich arenes **2** in the presence of molecular iodine and **PhI(OCOPh)$_2$**[a].

Entry	Arene **2**	Time (h)	Product **11**	Yield (%)[b]
1	 2a	72	 11a	69
2	 2b	72	 11b	67
3	 2c	73	 11c	56
4	 2d	76	 11d	27
5	 2e	76	 11e	23

[a]***Reaction conditions*:** Arene **2** (10.0 mmol), *p*-fluorophenylacetylene **10** (1.0 mmol), I_2 (1.25 mmol), $PhI(OCOPh)_2$ (3.0 mmol), CH_3CN (6.0 mL) at 82^oC.
[b]Isolated yield based on *p*-fluorophenylacetylene **10**.

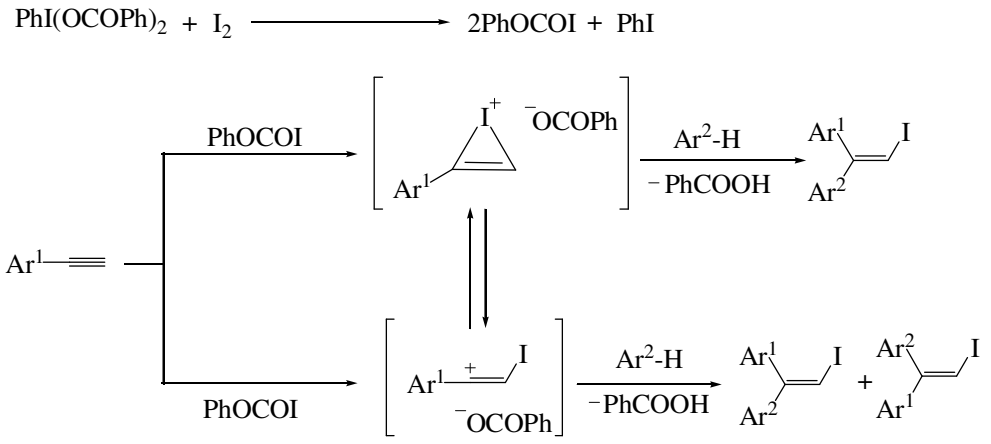
No iodoarylation reaction occurs with long chain aliphatic alkynes such as 1-hexyne and 3-butyn-2-one under the above reaction conditions, suggesting that this iodoarylation reaction is not applicable to aliphatic alkynes.

5.2.4. *Possible mechanism of the iodoarylation reaction*

The proposed mechanism of the iodoarylation reaction of arylacetylenes is shown in the **Scheme 13.** Initially, molecular iodine reacts with the oxidizing agent **PhI(OCOPh)$_2$** and forms a hypoiodite[9,10], **IOCOPh**. The resulting hypoiodite

reacts with arylacetylene and forms a cyclic iodonium ion. The cyclic iodonium ion then undergoes electrophilic aromatic substitution reaction with an electron rich arene and gives an iodoarylation product stereoselectively. In most cases, the cyclic iodonium ion is relatively more stable compared with an open chain vinyl cation due to a significant neighboring participation of the iodo group[11]. However, the open chain vinyl cation governs the reaction process in the case of 4-methoxyphenylacetylene, where the vinyl cation is highly stabilized by the electron releasing methoxyphenyl group and exists as an open chain form. The presence of the cyclic iodonium ion causes *trans* addition giving the stereochemically defined *trans* product. On the other hand, the open chain vinyl cation has a linear sp-hybridized structure and thus, an electron rich arene can attack from both sides of the vacant p-orbital of the open chain vinyl cation and gives a mixture of isomeric products. Accordingly, in the case of 4-methoxyphenylacetylene, an isomeric mixture of *E*- and *Z*-isomers is formed. The benzoate anion accepts a proton formed by the electrophilic aromatic substitution reaction and prevents the reaction from occurring by the protonation.

Scheme 13. Proposed mechanism of the iodoarylation reaction of alkynes



In this chapter it has been demonstrated that arylacetylenes undergo iodoarylation reaction with different electron rich arenes in the presence of a simple reagent system composed of molecular iodine and hypervalent iodine reagent, **PhI(OCOPh)$_2$**. The iodoarylation reaction of most arylacetylenes with electron

rich arenes proceeds regio- and stereoselectively to give *trans* 1,1-diaryl-2-iodoethene in good to high yields. In the case of 4-methoxyphenylacetylene, the iodoarylation reaction of 4-methoxyphenylacetylene with different electron rich arenes gives a mixture of *E*-and *Z*-isomers of 1,1-diaryl-2-iodoethenes **9 (Table 7).** No iodoarylation reaction occurs with long chain aliphatic alkynes. The method provides synthetically valuable iodoalkenes in the presence of a simple reagent system molecular iodine and hypervalent iodine compound, **$PhI(OCOPh)_2$**.

5.3. Experimental Section

General

All solvents and starting materials were used during the research works as received without further purification unless otherwise indicated. ^1H NMR and ^{13}C NMR were recorded on a JEOL JNM-Al-300FT-NMR (300 MHz) spectrometer in $CDCl_3$ solution (TMS as an internal standard). Melting points of the pure compounds were recorded by thin disc method on a YANACO melting point apparatus and are uncorrected. Column chromatographic separations were carried out using silica gel as the stationary phase. Pre-coated plates (silica gel $60F_{254}$, MERCK, on aluminum foils) were used for TLC examination. Elemental analysis was performed by the Service Center of the Elemental Analysis of Organic Compounds, Faculty of Science, Kyushu University, Fukuoka, Japan.

General procedure for the iodoarylation of alkynes

An arene (10.0 mmol), an alkyne (1.0 mmol), **I_2** (1.25 mmol), **$PhI(OCOPh)_2$** (3.0 mmol), and 6.0 mL of acetonitrile were taken in a 25.0 mL quick-fit round bottom flask. The reaction mixture was stirred for about 5 minutes at room temperature. The reaction mixture was then refluxed at 82^oC and stirred until the completion of the reaction. The reaction mixture was dissolved in 20.0 mL of dichloromethane, and 20.0 mL of water was added into the dichloromethane solution. The aqueous reaction mixture was extracted with dichloromethane (4 x 10.0 mL). The combined dichloromethane extract was washed with 1M sodium thiosulphate solution to remove the unreacted iodine. The dichloromethane extract was dried over anhydrous sodium sulfate. Finally, dichloromethane was removed under

reduced pressure below 40°C. Individual pure compounds were isolated by column chromatography on silica gel using hexane and dichloromethane as eluent.

***1-Iodo-2-(pentamethylphenyl)-2-(4-methylphenyl)ethene* 3a**

Yield: 0.3690g (86%); pale yellow viscous liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.37(d, *J* =7.8 Hz, 2H, Ar-H), 7.12(d, 2H, Ar-H, *J* =7.8 Hz), 6.31(s, 1H, =CH), 2.32(s, 3H, Me), 2.24(s, 3H, Me), 2.19(s, 6H, 2xMe), 2.15(s, 6H, 2xMe).

^{13}C NMR (75 MHz, $CDCl_3$): δ =151.31, 139.67, 137.68, 136.91, 134.41, 132.66, 131.33, 128.69, 128.49, 77.42, 21.29, 18.12, 16.80, 16.54.

Anal. Calcd. for $C_{20}H_{23}I$: C, 61.55; H, 5.94. Found: C, 61.54, H, 5.95.

***1-Iodo-2-(4-methylphenyl)-2-(2,4,6-trimethylphenyl)ethene* 3b**

Yield: 0.3111g (75%); pale yellow viscous liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.35(d, *J* = 8.1 Hz, 2H, Ar-H), 7.12(d, *J* =8.4 Hz, 2H, Ar-H), 6.85(s, 2H, Ar-H), 6.34(s, 1H, =CH), 2.32(s, 3H, Me), 2.27(s, 3H, Me), 2.14(s, 6H, 2xMe).

^{13}C NMR (75 MHz, $CDCl_3$): δ =149.62, 139.14, 137.83, 137.09, 136.50, 135.90, 128.68, 128.53, 128.43, 77.15, 21.30, 20.98, 20.33.

Anal. Calcd. for $C_{18}H_{19}I$: C, 59.68; H, 5.29. Found: C, 59.71, H, 5.32.

***1-Iodo-2-(4-methylphenyl)-2-(2,3,5,6-tetramethylphenyl)ethene* 3c**

Yield: 0.2365(56%); pale yellow viscous liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.37(d, *J* =8.1 Hz, 2H, Ar-H), 7.12(d, *J* =8.4 Hz, 2H, Ar-H), 6.92(s, 1H, Ar-H), 6.30(s, 1H, =CH), 2.32(s, 3H, Me), 2.20(s, 6H, 2xMe), 2.09(s, 6H, 2xMe).

^{13}C NMR (75 MHz, $CDCl_3$): δ =150.76, 142.05, 137.81, 136.69, 133.86, 131.81, 130.87, 128.72, 128.53, 76.70, 21.29, 20.08, 16.93.

Anal. Calcd. for $C_{19}H_{21}I$: C, 60.65; H, 5.63. Found: C, 60.68, H, 5.65.

***1-(3-Bromo-2,4,6-trimethylphenyl)-2-iodo-1-(4-methylphenyl)ethene* 3d**

Yield: 0.2093g (42%); pale yellow viscous liquid, mixture of *E*-and *Z*-isomers (E/Z ≈ 2).

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.35-7.07(m, Ar-H), 7.02(s, =CH), 6.94(s, Ar-H), 6.36(s, =CH), 2.44(s, Me), 2.39(s, Me), 2.32(s, Me), 2.30(s, Me), 2.23(s, Me), 2.11(s, Me), 2.02(s, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ =150.95, 149.58, 140.77, 140.14, 138.28, 138.18, 137.53, 135.96, 135.91, 135.46, 135.31, 134.68, 134.07, 129.99, 129.80, 129.45, 128.97, 128.63, 126.10, 125.62, 125.54, 81.11, 77.87, 24.11, 23.98, 21.77, 21.33, 21.18, 20.59, 20.18, 19.32.

Anal. Calcd. for $C_{18}H_{18}BrI$: C, 49.01; H, 4.11. Found: C, 48.96, H, 4.12.

1-(2,5-Dimethylphenyl)-2-iodo-1-(4-methylphenyl)ethene **3e**

Yield: 0.1161g (33%); pale yellow viscous liquid, mixture of *E*-and *Z*-isomers (E/Z ≈ 3).

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.28-7.00(m, Ar-H), 6.88(s, =CH), 6.49(s, =CH), 2.34(s, Me), 2.31(s, Me), 2.30(s, Me), 2.07(s, Me), 1.98(s, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ =152.28, 142.09, 141.70, 137.95, 137.72, 136.88, 135.33, 135.13, 132.59, 132.33, 130.46, 130.28, 130.11, 129.57, 129.19, 128.91, 128.65, 128.61, 126.54, 79.56, 78.02, 21.33, 21.15, 20.99, 20.82, 19.75, 18.86.

Anal. Calcd. for $C_{17}H_{17}I$: C, 58.64; H, 4.92. Found: C, 58.50, H, 4.91.

1-(2-methoxylphenyl)-2-iodo-1-(4-methylphenyl)ethene **3f**[4]

Yield: 0.1271g (35%); pale yellow colored waxy solid; Mp 101-102 ^{o}C. Mixture of *ortho*-, *meta*-, and *para*-isomers (20:20:60).

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.29- 6.75(m, 27H, Ar-H, and vinyl-H), 3.85(s, 3H, OMe), 3.79(s, 3H, OMe), 3.66(s, 3H, OMe), 2.39(s, 3H, Me), 2.35(s, 3H, Me), 2.32(s, 3H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ =159.51, 159.14, 159.04, 141.43, 137.77, 137.68, 136.57, 134.16, 130.82, 130.77, 129.72, 129.34, 129.25, 129.04, 128.99, 128.96, 128.83, 128.71, 128.50, 128.22, 127.60, 120.47, 113.64, 113.54, 111.57, 80.54, 77.18, 76.23, 55.62, 55.28, 55.19, 21.35, 21.30, 21.14.

1-Iodo-2-(pentamethylphenyl)-2-phenylethene **5a**[4]

Yield: 0.2734g (71%); pale yellow viscous liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.48-7.22(m, 5H, Ar-H), 6.37(s, 1H, =CH), 2.24 (s, 3H, Me), 2.20(s, 6H, 2xMe), 2.17(s, 6H, 2xMe).

^{13}C NMR (75 MHz, $CDCl_3$): δ =151.50, 139.88, 139.58, 134.58, 132.77, 131.39, 128.83, 127.86, 127.83, 77.64, 18.18, 16.83, 16.57.

1-Iodo-2-phenyl-2-(2,4,6-trimethylphenyl)ethene **5b**[4]

Yield: 0.2433g (61%); pale yellow viscous liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.45-7.21(m, 5H, Ar-H), 6.86(s, 2H, Ar-H), 6.41(s, 1H, =CH), 2.27(s, 3H, Me), 2.16(s, 6H, 2xMe).

^{13}C NMR (75 MHz, $CDCl_3$): δ =149.78, 139.46, 139.02, 137.22, 135.94, 128.82, 128.49, 127.96, 127.84, 78.01, 21.00, 20.38.

1-Iodo-2-phenyl-2-(2,3,5,6-tetramethylphenyl)ethene **5c**

Yield: 0.2428g (59%); pale yellow viscous liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.47-7.23(m, 5H, Ar-H), 6.94(s, 1H, Ar-H), 6.37(s, 1H, =CH), 2.21(s, 6H, 2xMe), 2.10(s, 6H, 2xMe).

^{13}C NMR (75 MHz, $CDCl_3$): δ =150.89, 141.89, 139.61, 133.93, 131.84, 130.95, 128.82, 127.93, 127.83, 77.60, 20.12, 16.98.

Anal. Calcd. for $C_{18}H_{19}I$: C, 59.68; H, 5.29. Found: C, 59.59, H, 5.30.

1-(3-Bromo-2,4,6-trimethylphenyl)-2-iodo-1-phenylethene **5d**

Yield: 0.1491g (32%); pale yellow viscous liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.45-7.24(m, 5H, Ar-H), 6.95(s, 1H, Ar-H), 6.43 (s, 1H, =CH), 2.38(s, 3H, Me), 2.33(s, 3H, Me), 2.12(s, 3H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ =149.72, 140.64, 138.91, 137.65, 135.93, 134.70, 129.85, 128.75, 128.21, 127.96, 125.66, 78.71, 23.98, 21.81, 20.21.

Anal. Calcd. for $C_{17}H_{16}BrI$: C, 47.80; H, 3.78. Found: C, 47.58, H, 3.75.

1-(2,5-Dimethylphenyl)-2-iodo-1-phenylethene **5e**[4]

Yield: 0.0864g (24 %); pale yellow colored highly viscous liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.39-6.98(m, 8H, Ar-H), 6.55(s, 1H, =CH), 2.32 (s, 3H, Me), 1.99(s, 3H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ =152.49, 141.94, 140.69, 135.19, 132.58, 130.49, 130.34, 129.04, 128.77, 127.93, 127.88, 78.74, 20.83, 19.78.

1-Iodo-2-(pentamethylphenyl)-1,2-diphenylethene **7a**

Yield: 0.0.0621g (14%); pale yellow colored crystalline solid, Mp 194.5-197°C.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.44-6.99(m, 10H, Ar-H), 2.20(s, 6H, 2xMe), 2.08(s, 3H, Me), 2.03(s, 6H, 2xMe).

^{13}C NMR (75 MHz, $CDCl_3$): δ =149.34, 144.94, 144.66, 137.66, 133.88, 132.35, 130.48, 129.37, 128.35, 127.64, 127.40, 127.31, 100.50, 18.80, 16.67, 16.49(one peak overlapped).

Anal. Calcd. for $C_{25}H_{25}I$: C, 66.38; H, 5.57. Found: C, 66.34; H, 5.59.

***1-Iodo-1,2-diphenyl-2-(2,4,6-trimethylphenyl)ethene* 7b**

Yield: 0.0.0327g (8 %); pale yellow colored crystalline solid, Mp 154-156°C.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.42-7.06(m, 10H, Ar-H), 6.64(s, 2H, Ar-H), 2.16(s, 6H, 2xMe), 2.13(s, 3H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ =147.55, 144.50, 144.19, 137.29, 136.77, 135.40, 129.52, 128.93, 128.39, 127.66, 127.60, 127.56, 127.42, 101.39, 20.92, 20.75.

HRMS-EI: m/z calcd. for $C_{23}H_{21}I$ $[M]^+$: 424.0688; Found: 424.0689.

***1-Iodo-2-(4-methoxyphenyl)-2-(pentamethylphenyl)ethene* 9a**

Yield: 0.3315g (75%); mixture of *E*-and *Z*-isomers (92:8); pale yellow colored crystalline solid, Mp 110-111.5°C.

^{1}H NMR (300 MHz ,$CDCl_3$): δ =7.42(d, Ar-H, *J* =9.0 Hz), 7.14(d, Ar-H, *J* =9.0 Hz), 7.02(s, 1H, vinyl-H), 6.82(d, Ar-H, *J* =9.0 Hz), 6.76(d, Ar-H, *J* =9.0 Hz), 6.24(s, 1H, vinyl-H), 3.78(s, 3H, OMe), 3.76(s, 3H, OMe), 2.28(s, 3H, Me), 2.23(s, 6H, 2xMe), 2.19(s, 6H, 2xMe), 2.14(s, 3H, Me), 2.04(s, 6H, 2xMe).

^{13}C NMR (75 MHz, $CDCl_3$): δ =159.29, 159.01, 152.24, 150.80, 139.69, 138.94, 134.20, 132.68, 132.46, 132.09, 131.34, 130.45, 130.30, 130.18, 129.52, 127.65, 113.84, 113.07, 79.28, 75.80, 55.20, 55.14, 18.06, 17.60, 16.94, 16.89, 16.80, 16.58.

HRMS-EI: m/z calcd. for $C_{20}H_{23}IO$ $[M]^+$: 406.0794; Found: 406.0791.

***1-Iodo-2-(4-methoxyphenyl)-2-(2,4,6-trimethylphenyl)ethene* 9b**

Yield: 0.2559g (63%); mixture of *E*- and *Z*-isomers (87:13); pale yellow colored higly viscous liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.36-6.76(m, Ar-H, and vinyl-H), 3.77(s, 6H, 2xOMe), 2.33(s, 3H, Me), 2.27(s, 3H, Me), 2.21(s, 6H, 2xMe), 2.06(s, 6H, 2xMe).

HRMS-EI: m/z calcd. for $C_{18}H_{19}IO$ $[M]^+$: 378.0481; Found: 378.0479..

1-Iodo-2-(4-methoxyphenyl)-2-(2,3,5,6-tetramethylphenyl)ethene **9c**

Yield: 0.2618g (62%); mixture of *E*- and *Z*-isomers (51:49); pale yellow colored crystalline solid, Mp 108-110^oC.

^1H NMR (300 MHz, $CDCl_3$): δ =7.36-6.77(m, Ar-H and vinyl-H), 3.78(s, 6H, 2xOMe), 2.25(s, 6H, 2xMe), 2.21(s, 6H, 2xMe), 2.14(s, 6H, 2xMe), 1.99 (s, 6H, 2xMe).

^{13}C NMR (75 MHz, $CDCl_3$): δ =159.37, 159.06, 157.94, 151.51, 144.75, 141.42, 134.16, 133.68, 133.40, 131.69, 131.05, 130.91, 130.83, 130.51, 130.15, 127.59, 113.89, 113.12, 79.04, 55.22, 55.16, 20.12, 20.11, 16.47, 15.82.

HRMS-EI: m/z calcd. for $C_{19}H_{21}IO$ $[M]^+$: 392.0637; Found: 392.0637.

1-(3-Bromo-2,4,6-trimethylphenyl)-2-iodo-1-(4-methoxyphenyl)ethene **9d**

Yield: 0.1496g (32%); mixture of *E*- and *Z*-isomers (58:42); pale yellow colored higly viscous liquid.

^1H NMR (300 MHz, $CDCl_3$): δ =7.81-6.68(m, Ar-H and vinyl-H), 3.86(s, 3H, OMe), 3.79(s, 3H, OMe), 2.45(s, 3H, Me), 2.38(s, 3H, Me), 2.37(s, 3H, Me), 2.21(s, 3H, Me), 2.16(s, 3H, Me), 2.01(s, 3H, Me).

HRMS-EI: m/z calcd. for $C_{18}H_{18}BrIO$ $[M]^+$: 455.9586; Found: 455.9583.

1-(2,5-Dimethylphenyl)-2-iodo-1-(4-methoxyphenyl)ethene **9e**

Yield: 0.0529g (16 %); mixture of *E*- and *Z*-isomers (60:40); pale yellow colored higly viscous liquid.

^1H NMR (300 MHz, $CDCl_3$): δ =7.76-6.73(m, Ar-H and vinyl-H), 3.86(s, 3H, OMe), 3.79(s, 3H, OMe), 2.33(s, 3H, Me), 2.32(s, 3H, Me), 2.21(s, 6H, 2xMe).

^{13}C NMR (75 MHz, $CDCl_3$): δ =159.08, 157.55, 157.22, 144.44, 143.91, 139.27, 136.44, 135.76, 131.30, 130.55, 130.43, 129.98, 129.93, 129.02, 128.78, 128.39, 113.40, 110.02, 85.30, 77.21, 56.33, 55.20, 20.97, 19.14, 19.09, 17.74.

HRMS-EI: m/z calcd. for $C_{17}H_{17}IO$ $[M]^+$: 364.0324; Found: 364.0327

1-(4-Fluorophenyl)-2-iodo-1-(pentamethylphenyl)ethene **11a**

Yield: 0.2741g (69 %); pale yellow viscous liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.44(dd, J = 8.9 Hz, $J_{H,F}$ =5.3 Hz, 2H, Ar-H), 6.98(t, $J_{H,H}$ = $J_{H,F}$ =8.9 Hz, 2H, Ar-H), 6.35(s, 1H, =CH), 2.24(s, 3H, Me), 2.19(s, 6H, 2xMe), 2.14(s, 6H, 2xMe).

^{13}C NMR (75 MHz, $CDCl_3$): δ =162.05(d, $^{1}J_{C,F}$ =247.5 Hz), 150.54, 139.34, 135.87, 134.72, 132.85, 131.27, 130.69(d, $^{3}J_{C,F}$ =8.1 Hz), 114.78(d, $^{2}J_{C,F}$ =21.8 Hz), 77.59, 18.10, 16.80, 16.55.

Anal. Calcd. for $C_{19}H_{20}FI$: C, 57.88; H, 5.11. Found: C, 57.96, H, 5.03.

1-(4-Fluorophenyl)-2-iodo-1-(2,4,6-trimethylphenyl)ethene **11b**

Yield: 0.2556g (67 %); pale yellow viscous liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.42(dd, J = 8.7 Hz, $J_{H,F}$ =5.4 Hz, 2H, Ar-H), 6.98(t, $J_{H,H}$ = $J_{H,F}$ =8.7 Hz, 2H, Ar-H), 6.86(s, 2H, Ar-H), 6.39(s, 1H, =CH), 2.27(s, 3H, Me), 2.14(s, 6H, 2xMe).

^{13}C NMR (75 MHz, $CDCl_3$): δ =162.09(d, $^{1}J_{C,F}$ =247.5 Hz), 148.78, 138.73, 137.35, 135.80, 135.40, 130.64(d, $^{3}J_{C,F}$ =7.8 Hz), 128.57, 114.82(d, $^{2}J_{C,F}$ =21.7 Hz), 78.06, 20.98, 20.31.

Anal. Calcd. for $C_{17}H_{16}FI$: C, 55.76; H, 4.40. Found: C, 55.79, H, 4.42.

1-(4-Fluorophenyl)-2-iodo-1-(2,3,5,6-tetramethylphenyl)ethene **11c**

Yield: 0.2202g (56 %); pale yellow crystalline solid, mp 102.7-104.5 ^{o}C.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.44(dd, $J_{H,H}$ =8.9 Hz, $J_{H,F}$ =5.4 Hz, 2H, Ar-H), 6.98(t, $J_{H,H}$ = $J_{H,F}$ =8.9 Hz, 2H, Ar-H), 6.93(s, 1H, Ar-H), 6.35(s, 1H, =CH), 2.20(s, 6H, 2xMe), 2.08(s, 6H, 2xMe).

^{13}C NMR (75 MHz, $CDCl_3$): δ =162.06(d, $^{1}J_{C,F}$ =248.1 Hz), 149.88, 141.61, 135.55(d, $^{4}J_{C,F}$ =3.1 Hz), 134.02, 131.72, 131.07, 130.67(d, $^{3}J_{C,F}$ =8.1 Hz), 114.80(d, $^{2}J_{C,F}$ =21.7 Hz), 77.61, 20.10, 16.92.

Anal. Calcd. for $C_{18}H_{18}FI$: C, 56.86; H, 4.77. Found: C, 56.75, H, 4.79.

1-(3-Bromo-2,4,6-trimethylphenyl)-1-(4-fluorophenyl)-2-iodoethene **11d**

Yield: 0.1260g (27%); pale yellow colored highly viscous liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.40-7.45(m, 2H, Ar-H), 7.01(t, $J_{H,H}$ = $J_{H,F}$ =8.7 Hz, 2H, Ar-H), 6.96(s, 1H, Ar-H), 6.42(s, 1H, =CH), 2.38(s, 3H, Me), 2.32(s, 3H, Me), 2.11(s, 1H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ =162.21(d, $^{1}J_{C,F}$ =248.1 Hz), 148.73, 140.35, 137.83, 135.85, 134.89(d, $^{4}J_{C,F}$ =3.1 Hz), 134.60, 130.62(d, $^{3}J_{C,F}$ =8.1 Hz), 129.91, 125.72, 114.98(d, $^{2}J_{C,F}$ =21.8 Hz), 78.76, 23.98, 21.75, 20.15.

Anal. Calcd. for $C_{17}H_{15}BrFI$: C, 45.87; H, 3.40. Found: C, 45.55, H, 3.30.

1-(4-Fluorophenyl)-2-iodo-1-(2,5-dimethylphenyl)ethene **11e**

Yield: 0.0901g (23%); pale yellow colored highly viscous liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.33-7.37(m, 2H, Ar-H), 6.99-7.05(m, 5H, Ar-H), 6.55(s, 1H, =CH), 2.32(s, 3H, Me), 1.96(s, 3H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ =162.09(d, $^{1}J_{C,F}$ =247.5 Hz), 151.50, 141.70, 136.60(d, $^{4}J_{C,F}$ =3.1 Hz), 135.31, 132.50, 130.90(d, $^{3}J_{C,F}$ =8.1 Hz), 130.46, 130.42, 128.91, 114.92(d, $^{2}J_{C,F}$ =21.1 Hz), 78.88, 20.80, 19.75.

Anal. Calcd. for $C_{16}H_{14}FI$: C, 54.57; H, 4.01. Found: C, 54.41, H, 3.98.

5.4. References

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CHAPTER 6

Direct Periodination and Selective Diiodination of Aromatic Compounds using Molecular Iodine

A Very Convenient, Simple Procedure for Iodoarenes from Simple Arenes

6.1. Introduction

Iodination of organic compounds and the chemistry of organic iodides are of interest as major chemical fields. Their industrial application is wide[1]. Iodination is one of the classical reactions of aromatic compounds and has been thoroughly investigated for both its theoretical and synthetic value. Aromatic iodo compounds are an important class of compounds in synthetic organic chemistry. They are useful for the preparation of organometallic reagents and some are potential intermediates for the synthesis of pharmaceutical and bioactive materials. They are also useful in metal-catalyzed coupling reactions which are widely applied in the preparation of complex molecules[2]. The iodination reaction of organic compounds using molecular iodine is particularly slower compared to chlorination and bromination and needs activation for effective electrophilic substitution.

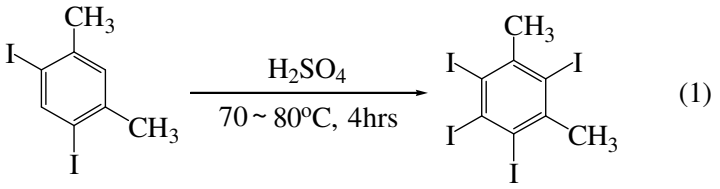
Since the molecular iodine is the least reactive among the halogens toward an electrophilic substitution process, most of the synthetic effort has been placed in converting molecular iodine into a more active species[3]. The iodination of aromatic compounds using molecular iodine is generally carried out only in the presence of a Lewis acid, a hydrogen iodide trap, or most commonly in the presence of an oxidizing agent[4]. The reagents reported for the iodination of aromatic compounds include use of N-iodosuccinimide (NIS)[5]; I_2/Ag_2SO_4[6]; I_2/Cr_2O_3[7]; I_2/TlOAc[8]; I_2/KI/$Hg(OAc)_2$[9]; NaOCl/NaI in aqueous alcohol medium[10]; NaI/chloramine-T in methanol[11]; and KI/HIO_4 in H_2SO_4[12].

In this dissertation the present research work has been confined on the direct periodination and selective diiodination of aromatic compounds using molecular iodine.

There exist a variety of routes for the direct periodination as well as the poly-iodination of aromatic compounds. Traditionally, poly-and periodinated aromatic compounds are prepared by time-consuming multi-step procedures from the corresponding amines involving acetylation, nitration, diazotization and reduction[13].

Suzuki *et al* reported the preparation of polyiodinated aromatic compounds directly from commercially available iodo compounds using sulfuric acid (**Scheme 1**)[14]. Their method is based on the migration of iodine atoms present in the nucleus of the aromatic iodo compounds (Jacobsen reaction)[15]. The scope of this method is very limited.

Scheme 1



(1)

There has been reported the preparation of periodinated aromatic compounds through the permercuration followed by iododemercuration with triiodide[16-17].

Lagowski *et al* reported the preparation of periodonaphthalene through the permercuration of naphthalene in molten mercury(**II**) trifluoroacetate (Equation 2 and **Scheme 2**), followed by iododemercuration using potassium triiodide in DMF (Equation 3 and **Scheme 2**)[18]. High temperature (180°C) is required to prepare permercurated naphthalene from naphthalene using mercury (**II**) trifluoroacetate and 7 days required to complete the demercuration reaction using potassium triiodide.

Scheme 2

$$C_{10}H_8 + 8Hg(O_2CCF_3)_2 + 4HgO \longrightarrow C_{10}(HgO_2CCF_3)_8 + 4Hg(O_2CCF_3)_2 + 4H_2O \quad (2)$$

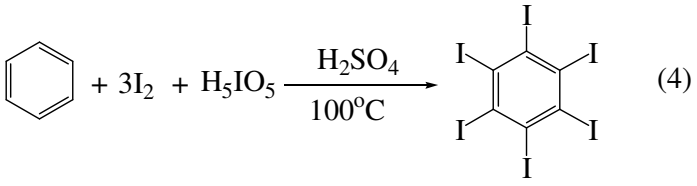
$$C_{10}(HgO_2CCF_3)_8 + 8I_3^- \longrightarrow C_{10}I_8 + 8HgI_2 + 8CF_3COO_2^- \quad (3)$$

It has already been mentioned that molecular iodine is not commonly used for the iodination of aromatic compounds due to its low electrophilic property. To carry out the direct iodination reaction using molecular iodine requires an appropriate oxidizing agent to convert molecular iodine into a powerful electrophile[19,20].

Preparation of periodinated aromatic compounds using molecular iodine in the presence of fuming sulfuric acid as an oxidizing agent under the influence of high temperature has been reported in the leterature[21,22].

Recently, Mattern[23] reported the preparation of periodinated aromatic compounds using molecular iodine in the presence of **H_5IO_6** in H_2SO_4 (**Scheme 3**). Initially, molecular iodine is converted into iodonium ion (**I^+**) in the presence of **H_5IO_6** and H_2SO_4 (Equation 5 and **Scheme 3**). The resulting iodonium ion then undergoes electrophilic aromatic substitution reaction with arene and gives periodination product. In H_2SO_4 the iodonium ion (**I^+**) largely disproportionates to **IO^+** and **I_3^+** ions. Thus, the identity of the actual electrophile is not certain.

Scheme 3



(4)

$$I_2 + H_5IO_5 + H_2SO_4 \longrightarrow I^+ + H_2O \quad (5)$$

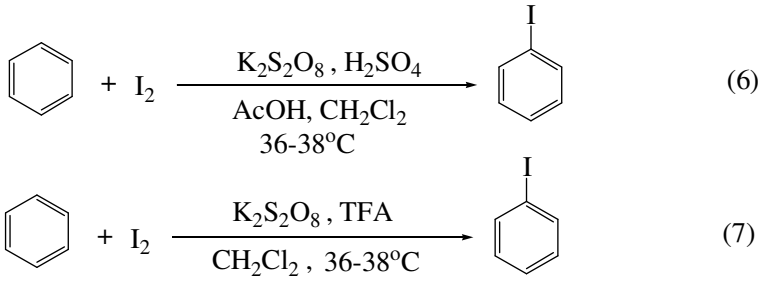
Although such reported methods for the preparation of iodoaromatic compounds are excellent and powerful in most cases, these methods have some drawbacks such as need longer reaction time and strong acidic or severe reaction conditions to carry out the reaction. Moreover, most of these iodinated reagents so far discussed are complicated, costly or use toxic heavy metal catalysts with potential environmental problems due to the generation of hazardous waste.

Therefore, it is desirable to seek an efficient, convenient, milder and environmentally benign procedure for the direct iodination of aromatic compounds.

Very recently, Kitamura *et al* reported that the direct iodination of aromatic compounds with molecular iodine proceeds smoothly in the presence of

potassium peroxodisulfate ($\mathbf{K_2S_2O_8}$) as an oxidant to give iodoarenes in good yields (**Scheme 4**)[24].

Scheme 4



This reagent system is convenient and powerful even in the case of deactivated arenes. Therefore, by extending the reported iodination method an attempt has been made to synthesize periodinated aromatic compounds and selective diiodo aromatic compounds using molecular iodine in the presence of $\mathbf{K_2S_2O_8}$, H_2SO_4 and trifluoroacetic acid in dichloroethane solvent. The present research work was, therefore, primarily aimed at preparing the periodinated and selective diiodinated aromatic compounds from simple arenes using molecular iodine.

The work was divided into two parts:

(a) ***Direct preparation of periodinated aromatic compounds*****, and**

(b) ***Selective diiodination of aromatic compounds***

Present periodination method is quite different from the previously reported periodination methods[21-23]. The present periodination method is effective for the arenes bearing moderately deactivating groups as well as the moderately activating groups. Moreover, the reaction conditions are milder than those of the reported periodination methods.

6.2. Results and Discussion

6.2.1. *Preparation of periodinated aromatic compounds*

Direct preparation of periodoarenes was carried out from the corresponding arenes using molecular iodine in the presence of $\mathbf{K_2S_2O_8}$, H_2SO_4 and trifluoroacetic acid in dichloroethane solvent under the influence of heat (**Scheme 5**). The present

periodination method is quite different from the previously reported periodination methods[21-23]. The present periodination method is effective for the arenes bearing moderately deactivating groups as well as the moderately activating groups. Moreover, the reaction conditions are milder than those of the reported periodination methods. The present periodination reaction has been studied to apply it to a variety of aromatic compounds. The results of the direct periodination of different arenes with molecular iodine in the presence of $\mathbf{K_2S_2O_8}$, H_2SO_4 and trifluoroacetic acid in dichloroethane solvent under the influence of heat are shown in **Table 1.**

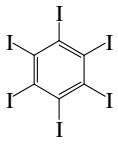
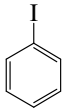
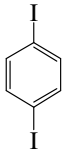
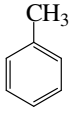
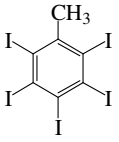
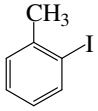
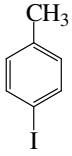
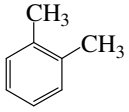
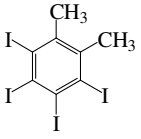
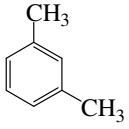
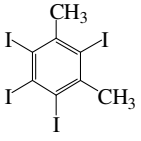
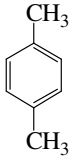
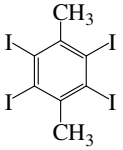
Scheme 5. Direct periodination of arenes using molecular iodine

(8)

R= H, CH_3, CH_3-CH_2, CH_3-$(CH_2)_2$-CH_2, F, Cl, Br, I

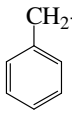
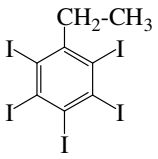
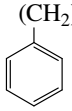
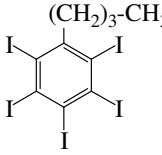
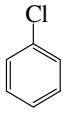
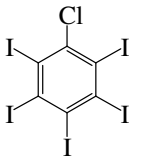
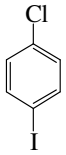
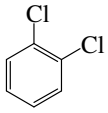
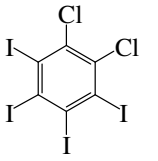
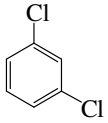
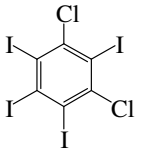
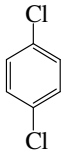
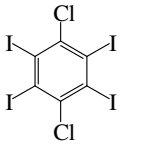
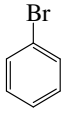
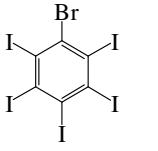
Aromatic compounds bearing weakly deactivating groups such as chloro, bromo, fluoro and iodo groups gave periodination products in good to high yields. Moderately activated aromatic compounds such as toluene, *o*-, *m*- and *p*-xylenes also gave periodination products in good to high yields. This method is not applicable for highly electron-rich aromatic compounds as well as for aromatic compounds bearing strongly electron-withdrawing groups. During the periodination of different aromatic compounds an excess amount of iodine was used to have the completely iodinated products. Benzene, iodobenzene and 1,4-diiodobenzene were easily converted into hexaiodobenzene (**1**) in high yields (Entries 1-3). The moderately activated arenes such as toluene, 2- and 4-iodotoluenes, *p*-xylene, ethylbenzene and butylbenzene were smoothly periodinated to give the products **2**, **5, 6** and **7** in high yields (Entries 4-6, 9, 11) except for ethylbenzene (Entry 10).

Table 1. Direct periodination of arenes using molecular iodine[a].

Entry	Arene	Temp.(°C)	Time(h)	Product	Yield(%)[b]
1		60	48	 **1**	89
2		60	48	**1**	87
3		60	48	**1**	90
4		30	36	 **2**	79
5		Rt	36	**2**	82
6		Rt	36	**2**	80
7		0-5	48	 **3**	53
8		0-5	48	 **4**	31
9		Rt	14	 **5**	70

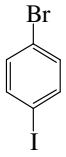
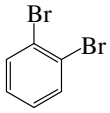
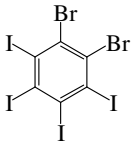
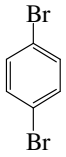
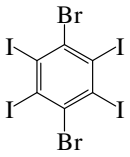
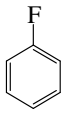
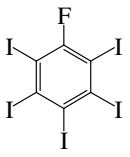
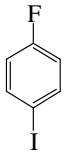
Continue

Table 1. Continue.

Entry	Arene	Temp.(°C)	Time(h)	Product	Yield(%)[b]
10		30	78	 **6**	36
11		Rt	48	 **7**	65
12		60	48	 **8**	86
13		60	24	**8**	88
14		60	48	 **9**	60
15		60	48	 **10**	87
16		60	36	 **11**	54
17		60	18	 **12**	97

Continue

Table 1. Continue.

Entry	Arene	Temp.(°C)	Time(h)	Product	Yield(%)[b]
18		60	36	**12**	87
19		60	18	 **13**	84
20		60	08	 **14**	86
21		45	60	 **15**	71
22		60	18	**15**	51

[a]***Reaction conditions***: Arene (1.0 mmo), **I_2** (5.0 mmol), $K_2S_2O_8$ (5.0 mmol), H_2SO_4 (1.0 mmol), TFA (4.0 mL), and dichloroethane (10.0 mL).

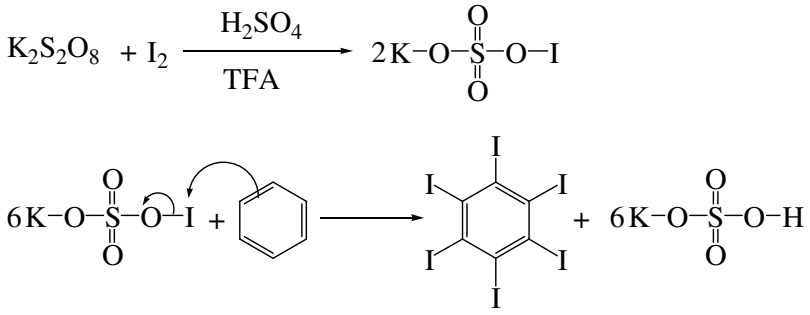
[b]Isolated yield.

Ethylbenzene gave 36% of periodinated product **6**. *o*-Xylene and *m* -xylene readily underwent periodination at low temperature but the yields were relatively lower than those of the periodination products of toluene, *p*-xylene and butylbenzene (Entries 7 and 8). The moderately deactivated aromatic compounds such as chlorobenzene, 1-chloro-4-iodobenzene, *o*-dichlorobenzene, *m*-dichlorobenzene, *p*-dichlorobenzene, bromobenzene, 1-bromo-4-iodobenzene, *o*-dibromobenzene, *p*-dibromobenzene, fluorobenzene and 4-fluoroiodobenzene were easily converted into the corresponding periodination products **8-15** (Entries 12-22) in good to high yields.

6.2.2. Mechanism of the periodination reaction of arenes

The possible mechanism of the periodination reaction of arenes is shown in **Scheme 6.** Initially, molecular iodine reacts with the oxidizing agent $\mathbf{K_2S_2O_8}$ in the presence of H_2SO_4 and trifluoroacetic acid and forms the iodonium ion source $\mathbf{KOSO_2\text{-}O\text{-}I.}$ The resulting iodonium ion source $\mathbf{KOSO_2\text{-}O\text{-}I}$ then undergoes electrophilic aromatic substitution reaction with an arene and gives periodination product.

Scheme 6. ***Probable mechanism of the periodination reaction of arenes***



In summary, a convenient and very simple method for the direct preparation of periodoarenes using molecular iodine has been demonstrated. This method covers many aromatic substrates including from moderately activated alkylbenzenes to moderately deactivated halobenzenes. Moreover, the periodination reaction proceeds under the mildest conditions among the procedures reported so far. Therefore, the present periodination method will be utilized for the synthesis of poly-functionalized materials.

6.2.3. ***Selective diiodination of aromatic compounds***

Selective diiodo aromatic compounds were prepared from the corresponding arenes using molecular iodine in the presence of $\mathbf{K_2S_2O_8}$, H_2SO_4 and trifluoroacetic acid in dichloroethane solvent under the influence of heat (**Scheme 7**).

In the present study, to optimize the iodination reaction initially, the work was concentrated on the efficiency of the diiodination of benzene using molecular

iodine in the presence of $\mathbf{K_2S_2O_8}$, H_2SO_4 and trifluoroacetic acid under different reaction conditins. The results are given in **Table 2**.

First of all, the reaction of benzene (1.0 mmol) with molecular iodine (1.0 mmol) in the presence of $\mathbf{K_2S_2O_8}$ (3.0 mmol), H_2SO_4(1.0 mmol), and trifluoroacetic acid, TFA (3.0 mL) in $(CH_2)_2Cl_2$ solvent (5.0 mL) at 40°C for 36 hours afforded a mixtures of 1,4-diiodo-, 1,2-diiodo- and other unidentified isomeric products **16** in 93% yield (Entry 1)**.** When the reaction of benzene (1.0 mmol) was carried out with molecular iodine (1.0 mmol) at 50°C for 36 hours afforded only a mixture of 1,4-diiodo- and 1,2-diiodobenzene in 82% yield (Entry 2). Again, when the reaction of benzene (1.0 mmol) was further carried out with increasing amount of molecular iodine (1.25 mmol), TFA (4.0 mL), and $(CH_2)_2Cl_2$ (10.0 mL) at 30°C for 18 hours gave an isomeric mixture of 1,4-diiodo- and 1,2-diiodobenzene in 15% yield of the product **16** (Entry 3). To improve the yield further the reaction of benzene (1.0 mmol) was carried out using different molar amount of molecular iodine under different reaction conditions (Entries 4-6). The best result (86%) was obtained when the reaction was carried out with benzene (1.0 mmol) in the presence of molecular iodine (1.11 mmol), $\mathbf{K_2S_2O_8}$ (3.0 mmol), H_2SO_4(1.0 mmol), and trifluoroacetic acid TFA (3.0 mL) in $(CH_2)_2Cl_2$ solvent (6.0 mL) at 50°C for 48 hours (Entry 4). Thus, the Entry 4 is the optimum condition for the reaction.

Scheme 7. Selective diiodination of benzene using molecular iodine

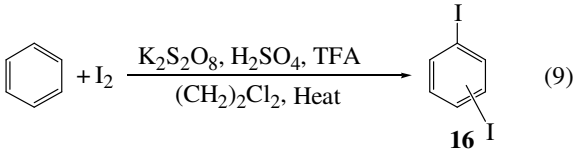


Table 2. Selective diiodination of benzene with molecular iodine[a]**.**

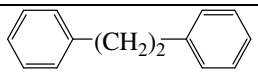
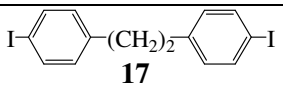
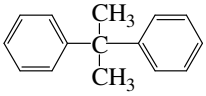
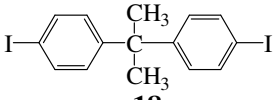
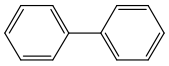
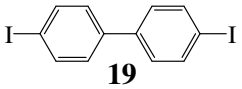
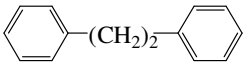
Entry	I_2(mmol)	$(CH_2)_2Cl_2$	Time (h)	Temp.(°C)	Product	Yield (%)
1	1.0	5(mL)	36	40	16	93
2	1.0	5(mL)	36	50	16	82
3	1.25	10(mL)	18	30	16	15[b]
4	**1.11**	**6(mL)**	**48**	**50**	**16**	**86**
5	1.11	6(mL)	15	60	16	58
6	1.25	6(mL)	48	40	16	85

[a]***Reaction conditions***: Benzene(1.0 mmol), $K_2S_2O_8$(3.0 mmol), TFA(3.0 mL), H_2SO_4 (1.0 mmol).

[b]TFA 4.0 mL was used.

Using the reaction conditions of the Entry 4 in **Table 2** the iodination reaction was further carried out with different biaryl compounds such as biphenyl, 2,2-diphenylpropane, and bibenzyl (Entry 1-3 and **Table 3**). In all cases the yields of the diiodo products **17-19** were very low. To improve the yield the reaction of bibenzyl was carried out using **$(NH_4)_2S_2O_8$** as an oxidant instead of **$K_2S_2O_8$** but the yield of the product **17** was also very low 18% (Entry 4). The reaction of bibenzyl was further carried out using different solvent systems such as nitrobenzene; mixture of nitrobenzene and dichloroethane (1:1); mixture of nitrobenzene, dichloroethane and acetic acid (1:1:1) under defferent reaction conditions but in all cases an unidentified complex mixture of products was formed. Again, the reaction of bibenzyl with molecular iodine in the presence of a mix solvent system such as dichloroethane, carbontetrachloride and acetic acid (1:1:1) under the reaction condition of the Entry 1 (**Table 3)** afforded a very low yield (12%) of the diiodo product **17**.

Table 3. Selective diiodination of different biaryl compounds with molecular iodine[a]

Entry	Arene	Time (h)	Product	Yield (%)[b]
1		36	 **17**	24
2		48	 **18**	16
3		72	 **19**	14
4		48	**17**	18[c]

[a]***Reaction conditions***: Arene(1.0 mmol), $\mathbf{I_2}$ (1.11 mmol), $K_2S_2O_8$ (3.0 mmol), TFA (3.0 mL), H_2SO_4 (1.0 mmol), $(CH_2)_2Cl_2$ (6 mL) at 50°C.

[b]Isolated yield.

[c]Oxidant $(NH_4)_2S_2O_8$ was used instead of $K_2S_2O_8$.

6.3. Experimental Section

General

All solvents and starting materials were used during the research works as received without further purification unless otherwise indicated. ^{1}H NMR and ^{13}C NMR were recorded on a JEOL JNM-AL-300FT-NMR spectrometer in DMSO-d_6 and $CDCl_3$ solution (TMS as an internal standard). Melting points of the pure compounds were recorded on a YANACO melting point apparatus and are uncorrected. Elemental analysis was performed by the Service Center of the Elemental Analysis of Organic Compounds, Faculty of Science, Kyushu University, Fukuoka, Japan.

(a) General procedure for the direct periodination of aromatic compounds

Required molar amount of arene (1.0 mmol), molecular iodine (5.0 mmol) and $\mathbf{K_2S_2O_8}$ (5.0 mmol) were dissolved in 10 mL of dichloroethane. The reaction mixture was stirred in an ice-water bath for about 5 minutes, and then were gradually added 4.0 mL of TFA and 1.0 mmol of sulfuric acid with constant stirring. The reaction mixture was stirred for about 10 minutes in the ice-water bath and stirred further for about 15 minutes at room temperature. The temperature of the reaction mixture was then gradually increased to the required temperature and stirred until the completion of the reaction. The reaction mixture was cooled, poured into ice-cold water, and then a solid precipitated. The resulting solid was collected by suction, washed with water and finally with dichloromethane or a mixture of dichloromethane and hexane to remove the unreacted iodine.

(b) General procedure for the selective diiodination of aromatic compounds

Required molar amount of biaryl compound (1.0 mmol), molecular iodine (1.11 mmol) and $\mathbf{K_2S_2O_8}$ (3.0 mmol) were dissolved in 6.0 mL of dichloroethane. The reaction mixture was stirred in an ice-water bath for about 5 minutes, and then were gradually added 3.0 mL of TFA and 1.0 mmol of sulfuric acid with constant stirring. The reaction mixture was stirred for about 10 minutes in the ice-water bath and stirred further for about 15 minutes at room temperature. The temperature of the reaction mixture was then gradually increased to the required temperature and stirred until the completion of the reaction. The reaction mixture was cooled and poured into 20.0 mL of water. The aqueous reaction mixture was extracted with dichloromethane (4 x 10.0 mL) and the combine dichloromethane extract was washed with 1M sodium thiosulphate solution to remove the unreacted iodine. Dichloromethane extract was dried over anhydrous sodium sulfate and finally, the dichloromethane was evaporated under reduced pressure below 40^{o}C. Individual pure compounds were isolated by column chromatography on silica gel using hexane as eluent.

Hexaiodobenzene **1**[23]

Yellow crystalline solid; Mp 355-375°C.

^{1}H NMR (300 MHz, DMSO-d_6): No signal in the ^{1}H NMR.

^{13}C NMR (75 MHz, DMSO-d_6): δ =121.65.

Pentaiodotoluene **2**[23]

Yellow crystalline solid; Mp 289-304°C.

^{1}H NMR (300 MHz, DMSO-d_6): δ =3.29(s, 3H, Me).

^{13}C NMR (75 MHz, DMSO-d_6): δ =147.06, 125.39, 119.52, 112.53, 47.05.

1,2,3,4-Tetraiodo-5,6-dimethylbenzene **3**[17]

Pale yellow crystalline solid; Mp 254-262°C.

^{1}H NMR (300 MHz, DMSO-d_6): δ =2.70(s, 6H, 2xMe).

^{13}C NMR (75 MHz, DMSO-d_6): δ =141.24, 121.69, 116.94, 33.78.

***1,2,3,5-Tetraiodo-4,6-dimethylbenzene* 4**[17]

Pale yellow crystalline solid; Mp 253-255°C**.**

^{1}H NMR (300 MHz, DMSO-d_6): δ =3.08(s, 6H, 2xMe).

^{13}C NMR (75 MHz, DMSO-d_6): δ =145.77, 126.93, 110.38, 104.42, 42.61.

***1,2,4,5-Tetraiodo-3,6-dimethylbenzene* 5**[17]

Light purple crystalline solid; Mp 237-243°C.

^{1}H NMR (300 MHz, DMSO-d_6): δ =3.23(s, 6H, 2xMe).

^{13}C NMR (75 MHz, DMSO-d_6): δ =145.29, 116.81, 46.02.

***Ethylpentaiodobenzene* 6**

Yellow crystalline solid; Mp 262-266°C.

^{1}H NMR (300 MHz, DMSO-d_6): δ =3.67(q, J =7.5 Hz, 2H, CH_2), 1.02(t, J =7.5 Hz, 3H, Me).

^{13}C NMR (75 MHz, DMSO-d_6): δ =151.58, 126.38, 120.20, 111.80, 50.86, 11.89.

Anal. Calcd for $C_8H_5I_5$: C, 13.06; H, 0.69. Found: C, 13.50; H, 0.78.

***Butylpentaiodobenzene* 7**

Pale yellow crystalline solid, Mp 157-159°C.

^{1}H NMR (300 MHz, DMSO-d_6): δ =3.75(t, J =7.5 Hz, 2H, CH_2), 1.60-1.39(m, 4H, CH_2CH_2), 0.98(t, J =7.2 Hz, 3H, Me).

^{13}C NMR (75 MHz, DMSO-d_6): δ =152.02, 125.12, 117.65, 110.34, 58.89, 29.36, 22.56, 13.71.

Anal. Calcd for $C_{10}H_9I_5$: C, 15.73; H, 1.19. Found: C, 15.89; H, 1.13.

***Chloropentaiodobenzene* 8** [23]

Yellow crystalline solid; Mp 323-331°C.

^{1}H NMR (300 MHz, DMSO-d_6): No signal in the ^{1}H NMR.

^{13}C NMR (75 MHz, DMSO-d_6): δ =140.02, 124.83, 120.90, 111.70.

***1,2-Dichloro-3,4,5,6-tetraiodobenzene* 9**

Yellow crystalline solid; Mp 275-308°C.

^{1}H NMR (300 MHz, DMSO-d_6): No signal in the ^{1}H NMR.

^{13}C NMR (75 MHz, DMSO-d_6): δ =133.74, 123.53, 115.04.

Anal. Calcd for $C_6Cl_2I_4$: C, 11.08. Found: C, 11.49.

***1,3-Dichloro-2,4,5,6-tetraiodobenzene* 10**

Yellow crystalline solid; Mp 258-262°C.

^{1}H NMR (300 MHz, DMSO-d_6): No signal in the ^{1}H NMR.

^{13}C NMR (75 MHz, DMSO-d_6): δ =142.74, 126.96, 111.18, 101.71.

Anal. Calcd for $C_6Cl_2I_4$: C, 11.08. Found: C, 11.34.

***1,4-Dichloro-2,3,5,6-tetraiodobenzene* 11**[25]

Pale yellow crystalline solid; Mp 248-275°C.

^{1}H NMR (300 MHz, DMSO-d_6): No signal in the ^{1}H NMR.

^{13}C NMR (75 MHz, DMSO-d_6): δ =139.27, 114.91.

***Bromopentaiodobenzene* 12**[16]

Yellow crystalline solid; Mp 316-325°C.

^{1}H NMR (300 MHz, DMSO-d_6): No signal in the ^{1}H NMR.

^{13}C NMR (75 MHz, DMSO-d_6): δ =134.29, 124.26, 121.34, 114.99.

***1,2-Dibromo-3,4,5,6-tetraiodobenzene* 13**

Yellow crystalline solid; Mp 260-272°C.

^{1}H NMR (300 MHz, DMSO-d_6): No signal in the ^{1}H NMR.

^{13}C NMR (75 MHz, DMSO-d_6): δ =129.28, 123.67, 117.58.

Anal. Calcd for $C_6Br_2I_4$: C, 9.75. Found: C, 10.15.

1,4-Dibromo-2,3,5,6-tetraiodobenzene **14**[25]

Pale yellow crystalline solid; Mp 271-285°C.

^{1}H NMR (300 MHz, DMSO-d_6): No signal in the ^{1}H NMR.

^{13}C NMR (75 MHz, DMSO-d_6): δ =133.86, 117.55.

Fluoropentaiodobenzene **15**[16]

Yellow crystalline solid; Mp 261-263°C.

^{1}H NMR (300 MHz, DMSO-d_6): No signal in the ^{1}H NMR.

^{13}C NMR (75 MHz, DMSO-d_6): δ =158.78(d, $J_{C,F}$ =239.9 Hz), 123.89, 117.58(d, $J_{C,F}$ =3.8 Hz), 96.41(d, $J_{C,F}$ =30.9 Hz).

1,4-Diiodobenzene **16**[24].

Yield: 0.2846g (86%); white color crystalline solid, Mp 126-128.4°C; mixture of 1,2-diiodo- and 1,4-diiodobenzene (7:93).

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.89-7.86(m, 2H, Ar-H), 7.05-7.02(m, 2H, Ar-H), 7.41(s, 4H, Ar-H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.43, 139.29, 129.13, 107.87, 93.34.

Recrystallization of the compound **16** from hot methanol yielded a white crystalline solid, yield: 0.2194g (66%); Mp 131.1-131.3°C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.40(s, 4H, Ar-H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.32, 93.33.

Melting point, ^{1}H NMR and ^{13}C NMR data revealed that the compound obtained from the recrystallization was pure 1,4-diiodobenzene.

4,4´-diiodobibenzyl **17**[26]

Yield: 0.1041g (24%); white crystalline solid, Mp 144.5-146.5°C.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.59(d, 4H, Ar-H, J = 8.7 Hz), 6.89(d, 4H, Ar-H, J =8.4 Hz), 2.83(s, 4H, 2xCH_2).

^{13}C NMR (75 MHz, $CDCl_3$): δ =140.77, 137.40, 130.56, 91.12, 37.04.

4,4´-diiodo-2,2-diphenylpropane **18**

Yield: 0.0720g (16%); white crystalline solid, Mp 102-104^{o}C.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.59(d, 4H, Ar-H, *J* = 8.4 Hz), 6.95(d, 4H, Ar-H, *J* = 8.4 Hz), 1.61(s, 6H, 2xCH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ =149.78, 137.17, 128.91, 91.26, 42.75, 30.37.

4,4´-diiodobipheny **19**

Yield: 0.0551g (14%); white crystalline solid, Mp 196-198^{o}C.

^{1}H NMR (300 MHz, $CDCl_3$): δ =7.77(d, 4H, Ar-H, *J* = 8.4 Hz), 7.29(d, 4H, Ar-H, *J* =8.4 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ =139.58, 138.01, 128.69, 93.49.

6.4. References

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CHAPTER 7

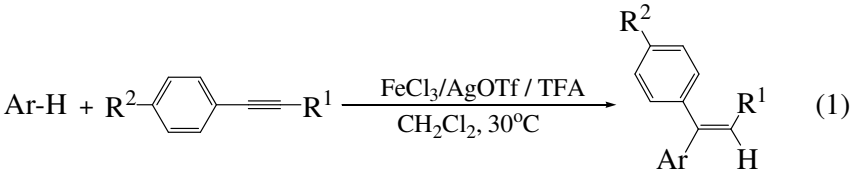
Summary

7.1. Summary

In this dissertation five different methods for direct functionalization of aromatic substrates have been developed. Of thses five deffrent methods four of them have been developed for the direct formation of new **carbon-carbon** bond between arenes and alkynes (**Chapter 2, 3 4** and **5**) and the fifth one has been developed for the direct iodination of aromatic compounds using molecular iodine (**Chapter 6**). All of these developed methods are important in the synthetic organic chemistry. The results obtained in this study are summarrized below:

In chapter 2, describes an effective, very simple, environmentally benign and efficient **$FeCl_3$/AgOTf** mediated hydroarylation reaction of arylsubstituted alkynes for the direct formation of new **carbon-carbon** bond between arenes and alkynes. In this modified developed method arylsubstituted alkynes smoothly undergo hydroarylation reaction with different electron rich arenes in the presence of **$FeCl_3$/AgOTf** catalyst in TFA and dichloromethane solvent at 30°C and afford 1,1-diarylalkenes in good to high yields (**Scheme 1**).

Scheme 1



(1)

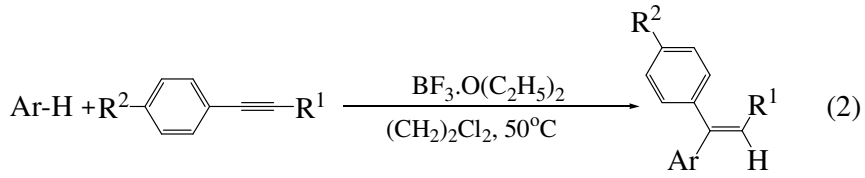
Ar = C_6H_5, $CH_3C_6H_4$, $C_2H_5C_6H_4$, $[(CH_3)_3C]_2C_6H_3$, $(CH_3)_2C_6H_3$, $(CH_3)_3C_6H_2$, $(CH_3)_3C_6HBr$, $(CH_3)_4C_6H$, $(CH_3)_5C_6$, $C_{10}H_7$

R^1= H, Ph, CH_3

R^2 = H, CH_3, F

In chapter 3, describes an effective, very simple **BF_3** mediated hydroarylation reaction of arylsubstituted alkynes for the direct formation of new **carbon-carbon** bond between arenes and alkynes. In this developed method arylsubstituted alkynes smoothly undergo hydroarylation reaction with different electron rich arenes in the presence of **BF_3** and dichloroethane solvent at 50°C and afford 1,1-diarylalkenes in moderate to good yields (**Scheme 2**).

Scheme 2



(2)

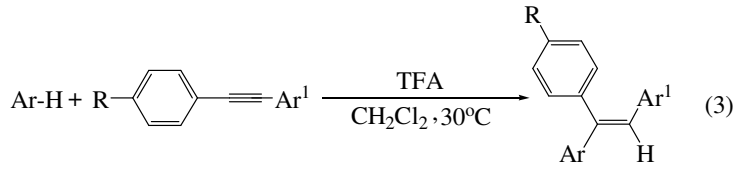
Ar = $(CH_3)_2C_6H_3$, $(CH_3)_3C_6H_2$, $(CH_3)_3C_6HBr$, $(CH_3)_4C_6H$, $(CH_3)_5C_6$

R^1= H, CH_3

R^2 = H, CH_3, F

In chapter 4, an efficient, simple, cheap, clean and environmentally benign **carbon-carbon** bond formation method has been developed using trifluoroacetic acid through the hydroarylation reaction without the involvement of transition metals or other additives. In this developed method arylsubstituted alkynes smoothly undergo hydroarylation reaction with different electron rich arenes in the presence of TFA catalyst in dichloromethane solvent at 30°C and afford 1,1-diarylalkenes in good to high yields (**Scheme 3**).

Scheme 3



(3)

Ar = C_6H_5, $CH_3C_6H_4$, $(CH_3)_2C_6H_3$, $[(CH_3)_3C]_2C_6H_3$, $(CH_3)_3C_6H_2$, $(CH_3)_3C_6HBr$, $(CH_3)_4C_6H$, $(CH_3)_5C_6$, $C_{10}H_7$

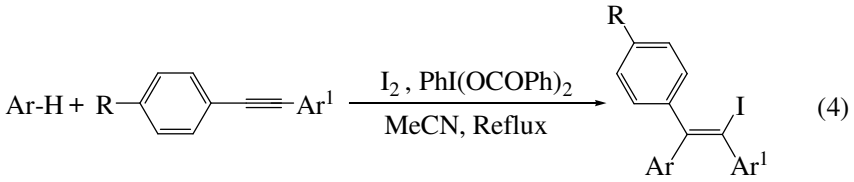
Ar^1= H, Ph

R = H, CH_3, OMe, F

In chapter 5, a new **carbon-carbon** bond formation method through the iodoarylation reaction between different electron rich arenes and arylsubstituted alkynes has been developed using molecular iodine in the presence of hypervalent iodine reagents in MeCN under the influence of heat without the involvement of metals or other addivies. Most arylsubstituted alkynes easily undergo iodoarylation reaction with different electron rich arenes to give *trans*-1,1-diaryl-2-iodoethene regio- and stereoselectively (**Scheme 4**). But an exceptional situation

arises in the case of *p*-methoxyphenylacetylene. *p*-Methoxyphenylacetylene undergoes iodoarylation reaction with different electron rich arenes and gives a mixture of *E*- and **Z**-isomers of the corresponding iodoarylated products. It is an effective, efficient, very cheap, simple, easy, and environmentally benign method for the direct formation of new **carbon-carbon** bond between electron rich arenes and arylsubstituted alkynes.

Scheme 4



(4)

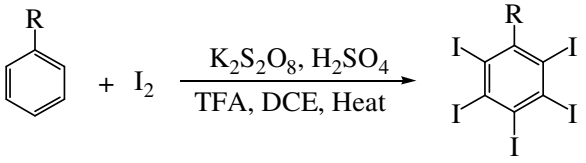
Ar = $(CH_3)_2C_6H_3$, $(CH_3)_3C_6H_2$, $(CH_3)_3C_6$ HBr, $(CH_3)_4C_6H$, $(CH_3)_5C_6$

Ar^1 = H, Ph

R = H, CH_3, OMe, F

In chapter 6, finally, an effective and efficient method has been developed for the direct preparation of periodinated aromatic compounds and selective diiodo aromatic compounds using molecular iodine in the presence of potassium peroxodisulfate in TFA, H_2SO_4 and dicloroethane solvent. The reaction of arenes (1.0 mmol) with molecular iodine (5.0 mmol) in the presence of potassium peroxodisulfate, $\mathbf{K_2S_2O_8}$ (5.0 mmol), TFA (4.0 mL), H_2SO_4 (1.0 mmol) in dicloroethane (DCE) solvent afford periodinated aromatic compounds in good to high yields (**Scheme 5**).

Scheme 5

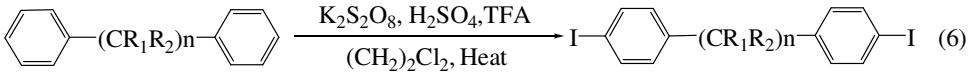


(5)

R= H, CH_3, CH_3-CH_2, CH_3-$(CH_2)_2$-CH_2, F, Cl, Br, I

On the other hand, the reaction of arenes (1.0 mmol) with molecular iodine (1.11 mmol) in the presence of potassium peroxodisulfate, $\mathbf{K_2S_2O_8}$ (3.0 mmol), TFA (3.0 mL), H_2SO_4 (1.0 mmol) in dicloroethane solvent afforded selective diiodo aromatic compounds (**Scheme 6**). Unfortunately the yields of the resulting diiodo compounds were not so encouraging.

Scheme 6



(6)

(i) n = 0 ; (ii) n =1, $R_1 = R_2 = CH_3$; and (iii) n = 2, $R_1 = R_2 = H$

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Md. Ataur Rahman

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